THE American Journal OF Gastroenterology

VOL. 25, NO. 2 FEBRUARY, 1956

Pathologic Anatomy of Massive Hemorrhage in Peptic Ulcer

Nausea and Vomiting, Without Abdominal Pain, Due to Giardiasis

Special Gastroenterological Diagnostic Procedures

Present Status of Portal Decompression for Portal Hypertension

The Effects of a Low Fat Diet on the Incidence of Gallbladder Disease

Third Annual Convention
New York, N. Y.
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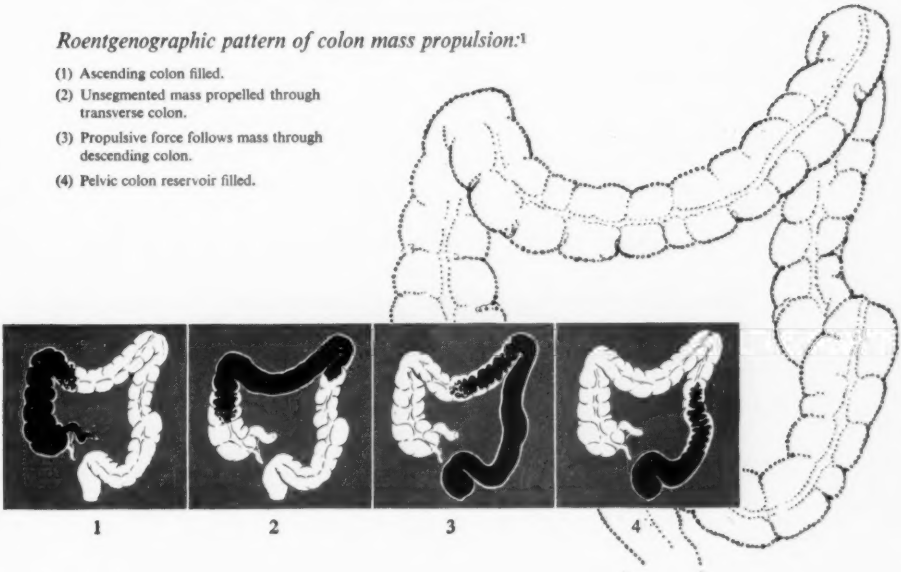

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The American Journal of Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

Editorial Board and General Information 100
Pathologic Anatomy of Massive Hemorrhage in Peptic Ulcer
MILTON G. BOHROD, M.D. 109
Lymphatic Leukemia Complicated by Carcinoma of the Stomach
ABRAHAM J. BRENNER, M.D., F.A.C.G. and
BERNARD S. EPSTEIN, M.D., F.A.C.R. 116
Emphysematous Gastritis ..... BERNARD FARFEL, M.D. and
RALPH EICHHORN, M.D., F.A.C.G. 125
Nausea and Vomiting, Without Abdominal Pain, Due to Giardiasis
MICHAEL WEINGARTEN, M.D., F.A.C.G. and JESSE J. SERWER, M.D. 131
Special Gastroenterological Diagnostic Procedures..... J. ALFRED RIDER,
M.D., Ph.D., LEO VAN DER REIS, M.D. and JENNIE LEE, M.D. 137
Present Status of Portal Decompression for Portal Hypertension
CHARLES G. CHILD, III, M.D. 148
Diverticulosis of the Gallbladder.... D. P. HALL, M.D., F.A.C.S., F.A.C.G. 154
The Effects of a Low Fat Diet on the Incidence of Gallbladder Disease
LESTER M. MORRISON, M.D., F.A.C.G. 158
Some Perplexities in the Problem of Jaundice... LOUIS J. VORHAUS, II, M.D. 164
The Association of Liver Disease with Ulcerative Colitis... HARRY J. KANIN,
M.D., JACK J. LEVIN, M.D., F.A.C.G. and M. C. F. LINDERT, M.D. 172
Editorials:
"Irritable Colon"—A Bad Term.... ANTHONY BASSLER, M.D., F.A.C.G. 176
Improved Anesthesia For Gastroscopy
MILTON J. MATZNER, M.D., F.A.C.G. 177
In Memoriam 177
President's Message 178
News Notes 179
Program, Southern Regional Meeting 180

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Index to Advertisers

Ames Co., Inc. 108
Arlington-Funk Laboratories 102
Astra Pharmaceutical Products, Inc..... 185
Borden Co., The 104
Brayten Pharmaceutical Co..... 3rd cover
Ciba Pharmaceutical Products, Inc..... 103
Desitin Chemical Co. 190
Endo Products, Inc. 182
Fleet, C. B., Co., Inc. 184
Hoffmann-La Roche, Inc. 98
Horlicks Corp. 186
Lakeside Laboratories, Inc. 191
National Drug, Co., The 105
Pfizer Laboratories 192
Photovolt Corp. 186
Rorer, William H., Inc. 187
Schering Corp. 183
Searle, G. D. & Co. 97
Sharp & Dohme ..... 189, 2nd cover
Standard Pharmaceutical Co., Inc..... 186
Upjohn Co. 106
U. S. Treasury 188
Warner-Chilcott Laboratories ..... 4th cover
Winthrop Laboratories, Inc. 107
Wyeth, Inc. 101

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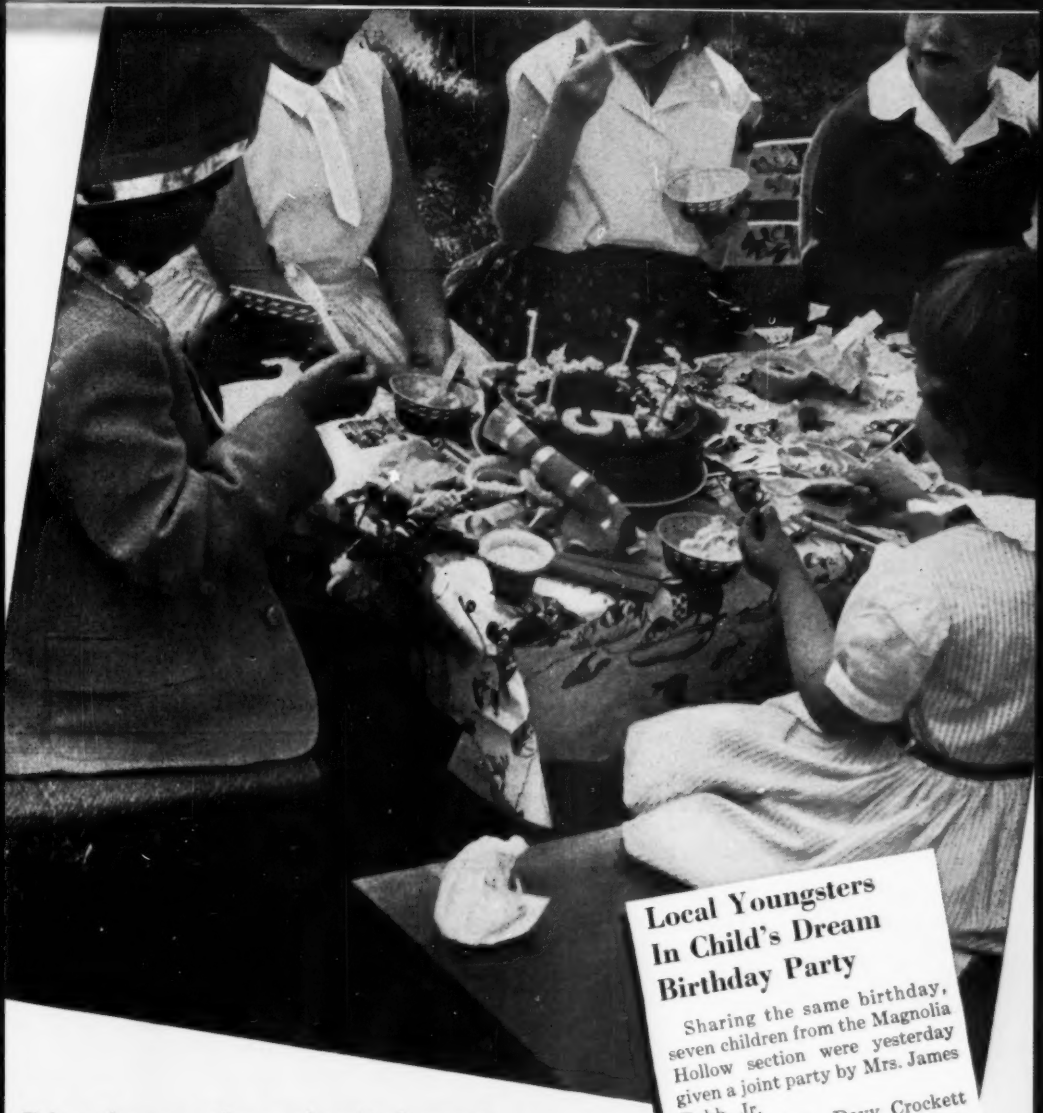

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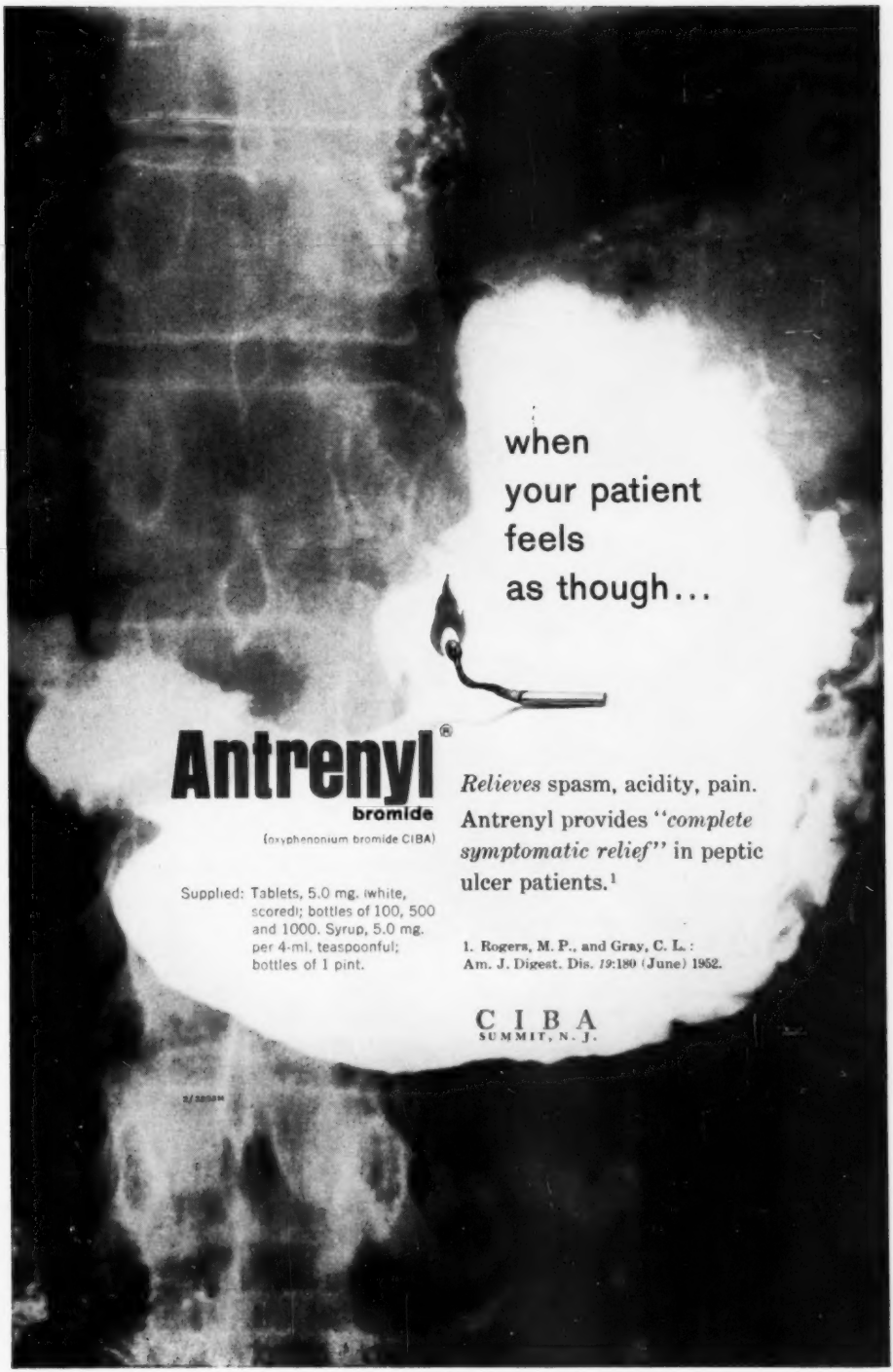
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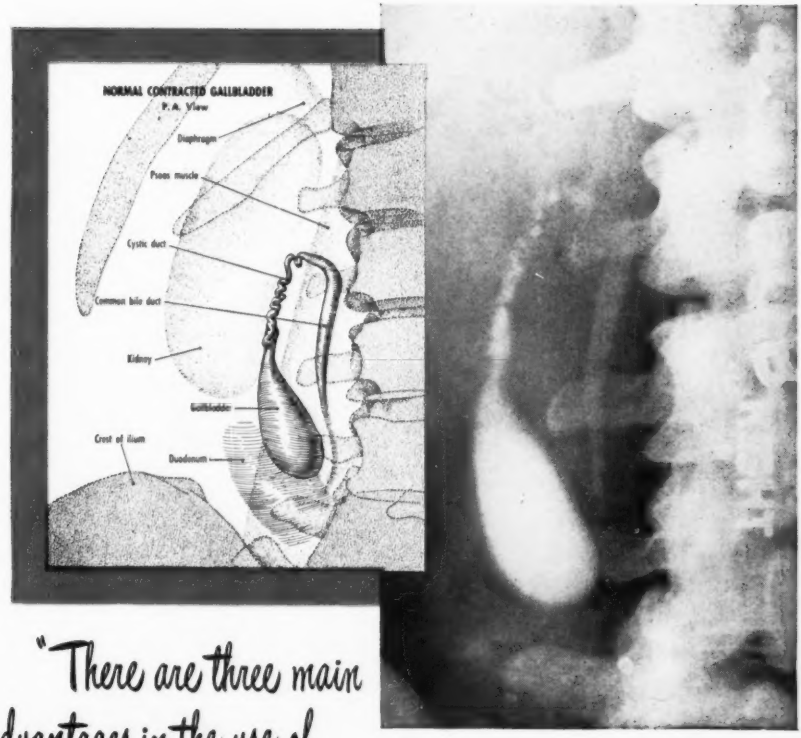

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VOLUME 25 FEBRUARY, 1955 NUMBER 2

PATHOLOGIC ANATOMY OF MASSIVE HEMORRHAGE IN PEPTIC ULCER*

WITH A CONSIDERATION OF THE THERAPEUTIC MORAL

MILTON G. BOHROD, M.D.†

Rochester, N. Y.

About 20 years ago Dr. Arthur Hertzler, the "Horse and Buggy Doctor", said at a county medical society meeting that he had never seen a death from hemorrhage of a peptic ulcer. From all sides of the auditorium doctors directed looks and winks at me, the only pathologist in town, until I felt I ought to say something in the discussion period. What I said was that I had always believed that the couple of dozen such cases on which I had performed necropsies had been dead before I started the examination. Dr. Hertzler wisecracked something about the advantage of the climate of Kansas over that of Illinois.

This little incident contains in it indications for two important considerations. First it points to a difficulty about statistics. Dr. Hertzler's patients were not a typical sample of bleeding peptic ulcers. He worked in a small town, Halstead, Kansas, and most of his surgical patients were referred from a distance. The kind of patients who died in hemorrhage were not the kind who could be transported by auto or train to his clinic. The second consideration is the one which is the major concern of this paper: it is that there are at least two kinds of hemorrhage in peptic ulcers and the anatomy of each is different from the other. The one is susceptible to medical management; the other, I contend, can be and must be treated surgically.

The mortality statistics in severe hemorrhage in peptic ulcer show a remarkable uniformity in different parts of our country and in different countries in the world. There are two general ways of expressing them. One is to say that 89 per cent of cases (plus or minus 2 or 3 per cent) respond to medical

*Read before the Second Annual Convention of the American College of Gastroenterology, Chicago, Ill., 24, 25, 26 October 1955.

†Pathologist and Director of Laboratories, Rochester General Hospital, Rochester, N. Y.

management. The other is to say that 11 per cent die. The urgency with which one approaches the problem depends in part upon which one of these ways is used for expressing the facts.

The commonest mechanism for hemorrhage from a peptic ulcer is by diapedesis through capillaries, no doubt at times aided by rupture of capillary vessels. Hemorrhages produced in this way can be very severe. As a matter of fact, severe and even occasionally fatal hemorrhage by diapedesis can occur through the intact, nonulcerated stomach mucosa, an event which used to be not too rare in severe acute infections, especially pneumonia. Similar severe hemorrhages by diapedesis may occur from other mucous membranes. I have seen them from the urinary bladder and the rectum. Increased tendency to bleed for any reason whatever increases both the frequency and the severity of the hemorrhage. The first hours of a massive hemorrhage may seem clinically identical in this type and in the type described below. It is in this first type

Fig. 1—Probes inserted into the proximal and distal openings in the ruptured artery in the base of a duodenal ulcer.

that recovery may be prompt even after a very brisk hemorrhage. It is here that blood transfusions act not only as replacement for lost blood but to diminish the bleeding time. Here one may also like to remember that a small amount of *fresh* blood has a much greater influence on clotting and bleeding time than a much larger amount of bank blood.

The second type of massive hemorrhage in peptic ulcer is caused by erosion into a large blood vessel, usually a branch of the duodenopancreatic artery. This is almost invariably the type seen in fatal cases. The pathologic anatomy in these cases is strikingly constant. In almost all cases the ulcer is in the first two-thirds of the duodenum and lies in the posterior wall over the pancreas. It has been my custom for years to emphasize this point during a necropsy by opening the anterior wall of the duodenum at the very beginning of the examination and immediately disclosing the ulcer and the bleeding vessel. My

surgeon-colleague Dr. Donald Houghton has been doing the same thing in the operating room, and for several years now, since the moral of the anatomical data has been appreciated he and other surgeons' opportunities to make this demonstration has increased while mine has, *pari passu*, greatly diminished.

A probe inserted into the bleeding point can be pushed in two different directions (Fig. 1), indicating that the perforation of the vessel is lateral. In some cases a longer segment of wall has been eroded, and two openings are found into each of which a probe can be passed. In almost every case, however, a portion of the posterior wall of the artery can still be made out (Fig. 2) again emphasizing the point that the erosion is lateral. A careful, or perhaps a lucky cut of a specimen along the longitudinal axis of the vessel (Fig. 3) shows the lateral blow-out and the relation to ulcer and pancreas very clearly.

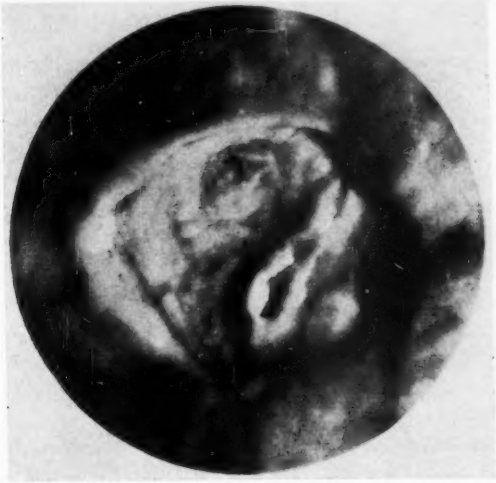

Fig. 2—View of the top of a ruptured artery showing the two openings and the remaining inferior wall of the vessel.

Complete transection of the vessel may occur (Dr. Houghton tells me he saw it once in the operating room) but I have never seen it. This is relevant to some of the misconceptions which, until recently at least, have been prevalent about the pathologic anatomy of massive hemorrhage in peptic ulcer. Because this type of bleeding occurs mostly in older people and because many of these same persons have arteriosclerosis, it was felt that the sclerosis in some way prevented the retraction of the artery and the consequent spontaneous closure. The rigid scar tissue in the floor of the ulcer no doubt contributed. But arteriosclerosis, no matter how prevalent in other parts of the body, is not notable in the area of the ulcer. Indeed, it has been shown that the arteries in this

region are rather immune to sclerosis. Since, however, the perforation of the vessel is lateral, any tendency of the vessel to retract would cause the opening to gape and keep it open longer. There seems to be no actual relation between arteriosclerosis and massive bleeding from peptic ulcer except that both sclerosis and very chronic ulcers tend to occur in older people.

Closer study shows, at the periphery, the destruction of the supporting structures of the vessel wall, muscle and especially elastic tissue (Fig. 4). Presumably these are the earliest important changes in the center of the lesion, although by the time the hemorrhage occurs this portion of the vessel may be completely destroyed. It seemed likely from analogy with similar vascular lesions, however, that when the supporting elastic tissue is damaged by the advancing front of the eroding ulcer, an aneurysm would be formed which would protrude into the floor of the ulcer. For some years we have been on the look-out for such a lesion and recently we found one (Fig. 5): a recent

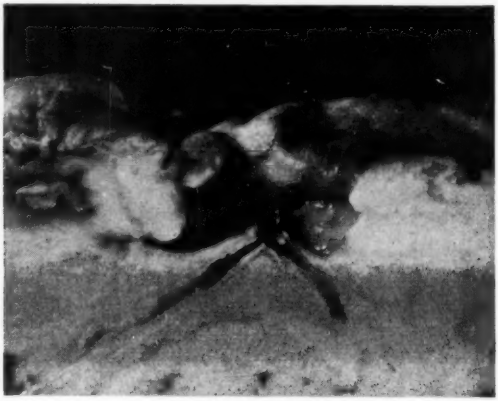

Fig. 3—Longitudinal section of a ruptured artery. Note the *lateral* rupture and the relation to the pancreas, below.

rupture in which the aneurysm was still easily visible. If this is the mechanism, as seems probable, it is easily apparent that trauma of coarse duodenal contents or moments of increased blood pressure might play a part in determining just when the aneurysm would rupture and bleeding ensue.

The great constancy of location and anatomy in massive hemorrhage due to ruptured artery has already been mentioned. One of our cases which is an apparent exception emphasized this. The patient died after a massive hemorrhage and after many transfusions. The ruptured vessel was not in the duodenum, nor was the ulcer. Both were in the stomach. But an anomaly caused the pancreas to lie beneath the stomach in this instance, and the relations among

ulcer, pancreas, and pancreatico-"duodenal" artery was the same as in the usual case.

If massive hemorrhages of this sort are, then, due to lateral perforation of a branch of the pancreaticoduodenal artery, probably the blowout of an aneurysm in the floor of the ulcer, the proper treatment is immediately apparent. The artery in this location is about the same size as the radial artery. When a medical treatment is devised for a ruptured radial artery, pretty much the same treatment can be used for the duodenal lesion. Until then, the treatment will have to be, as with the lesion of the radial artery, surgical. No one who has carefully examined a pathologic specimen and probed the affected vessel can have much doubt concerning this conclusion.

The precise kind of surgical intervention will be determined by many factors and have been discussed by many surgeons.* Only one point needs to be made here. Ligation of vessels on the outside of the duodenum or stomach is futile; there are too many anastomosing vessels. It is necessary to open the

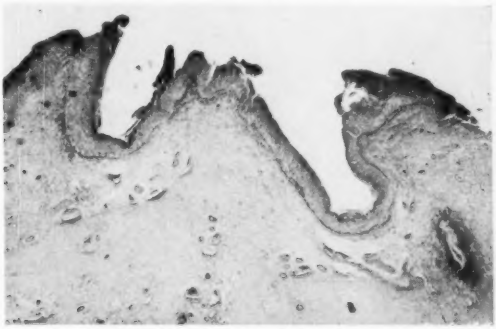

Fig. 4—Low power photomicrograph of a partially longitudinal section. Because of bends in the vessel the continuations of the artery to right and left are not visualized. Elastic tissue stain.

duodenum and stop the bleeding from the inside. Resections of one sort or another may or may not be done afterwards.

If we are agreed, then, that there are two types of severe bleeding in peptic ulcer, by diapedesis or capillary ooze, and by rupture of an artery, and that the treatment of the first may be medical but that the treatment of the second must be surgical, we are left with the crux of the problem: How do you tell which type a given patient has? This can be a very difficult matter† and may

*The experiences and opinions from our hospital will be reported by Dr. Houghton.

†There are of course other causes for severe upper gastrointestinal hemorrhage and their differentiation may be difficult and is always important. What is stressed here starts with the assumption that the seat of the bleeding has been determined to be very probably in a peptic ulcer.

at times be impossible. But the proper question often goes a long way toward achieving a proper solution; and the appreciation that two types exist is necessary before the differentiation can be made. Only the principles for such differential diagnosis can be discussed here.

Several criteria used in the past for determining when a patient with massive bleeding should be operated on can be applied here. These have included the reaction to a certain number of transfusions or within a time limit (Finsterer's 48-hour rule, for instance). I like the following: Whenever it becomes apparent that the patient is losing blood about as fast as you are giving it to him—operate. Usually it does not take more than a very few units of blood to find out, two or three. These units should be given, not according to a predetermined time schedule, but according to the clinical judgment of the need of the patient for blood. In this way it is possible to determine the indication for surgical intervention sometimes in a few hours, in most cases within 24-48 hours.

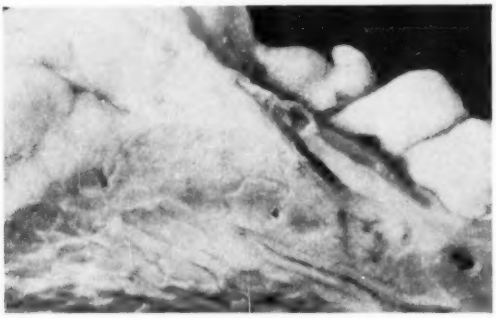

Fig. 5—Partial longitudinal section of artery showing an aneurysm projecting into the floor of the ulcer above. Note the pancreas below.

If the patient is losing blood as fast as he is getting transfusions, it is futile to withhold operation until clinical improvement occurs. Most of the necropsies I now see in cases of bleeding of this sort are on patients who died while they were in the process of being "built-up". A man is just as dead if he dies in a hospital bed as if he dies on an operating table. A certain amount of risk must be taken; it will be less in instances of this kind, than the risk of temporizing. A single unit of blood given after the bleeding point has been closed will often do more good than large amounts given before. My surgical colleagues assure me that even the mere stopping of the hemorrhage, for instance by a mattress suture, often causes immediate improvement in blood pressure and other features; and that a very short wait, and even fairly small amounts of blood given after the bleeding is controlled often allows operations as severe as subtotal gastrectomy to be performed at the same sitting.

Summary

1. There are two types of severe hemorrhage in peptic ulcer. One is by diapedesis or small capillary rupture, or both, and is generally controllable by medical management. This group makes up the bulk of the cases. The second type is a rupture of a medium-sized artery and the control of this type must be surgical.

2. Rupture of an artery which gives rise to massive hemorrhage occurs nearly always in that part of the duodenum which lies over the pancreas. The advancing ulcer damages the muscle and elastic tissue of the vessel, an aneurysm is produced, and the aneurysm ruptures.

3. Arteriosclerosis has nothing to do with this process. The opening in the vessel is lateral, and the failure to close is not due to failure to retract but is in part maintained by retraction.

4. The treatment of such a blowout in the lateral wall of a vessel can only be surgical.

5. The hardest problem is the differentiation of the two types of severe hemorrhage. It is proposed that the following rule be used as an indication for surgical intervention: Whenever it is apparent that the patient is losing blood about as fast as he is getting it in the form of transfusions—operate.

LYMPHATIC LEUKEMIA COMPLICATED BY CARCINOMA OF THE STOMACH

ABRAHAM J. BRENNER, M.D., F.A.C.G.*
Brooklyn, N. Y.
and
BERNARD S. EPSTEIN, M.D., F.A.C.R.†
New Hyde Park, N. Y.

While infrequent, the coexistence of leukemia and carcinoma may be anticipated to increase as the life expectancy of the population advances. Chronic lymphatic leukemia, especially in older people, may be implicated more often because of the greater frequency of malignant disease in this age group. There are some reports in the literature on this subject by Morrison, Feldman and Samwick[1] and Bichel[2]. The latter suggests a somewhat charac-

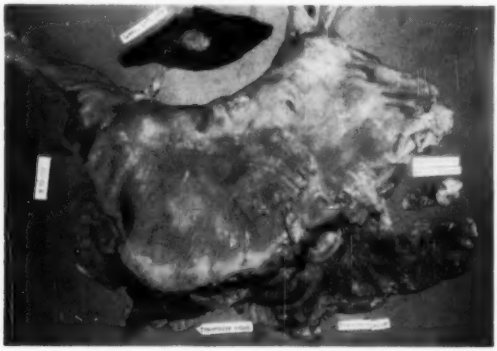

Fig. 1—Stomach wall adherent to the transverse colon with gastrocolic fistula.

teristic behavior of chronic lymphatic leukemia when complicated by carcinoma in that the leukemic picture recedes as the malignancy progresses. Contrary to Bichel's findings, however, at necropsy our case revealed marked visceral manifestations of leukemic infiltration.

Case Report

E. S., a 57-year old white male, was first seen on January 29, 1952 because of dysphagia, abdominal cramps, sour eructations, anorexia, weakness and loss of weight for six months. This had become more pronounced in the past two

From the Gastrointestinal Service, Jewish Hospital of Brooklyn.
*Assistant Gastroenterologist, Jewish Hospital of Brooklyn.
†Chief, Department of Radiology, Long Island Jewish Hospital.

TABLE I

Date	Hb.	R.B.C.	W.B.C.	Polys.	Bands	Lymph.	Monos.	Eosin.	Baso.	Platelets	Remarks
1952											
1-30	80	4.19	22,250	16	5	72	3	4	1	Normal	27 smudges per 100 W.B.C.
2-1	78	4.5	23,000	7	1	92					X-ray therapy begun 2-6-52
2-8	74	4.15	20,000	33	10	54		3			
2-13	65	3.8	8,400	62	20	16		2			
2-15	73	3.79	4,900	56	8	30	5	1			Hematocrit: 35 per cent packed cells
2-19	73	3.79	5,500	58		39	2	1			
2-21	77	3.72	6,850	57	9	30	2	2			
2-25	81	4.11	5,200								
3-31	70	4.2		40	15	40		4	1		Urethane therapy begun. Normal differential. No abnormal cells seen.
4-7	40	2.2	7,000								
6-16	70	4.5	10,150	43	15	38	1	2	1	Normal	1 myelocyte
6-30	77	3.75	7,100	33	34	19	6	5	2	275,000	
8-17	72	3.9	16,000	43	15	38	1	2	1	Normal	
8-25			8,000	80		18	2			Normal	T.E.M. Therapy begun.
8-29			5,000	81		15	2	2		Normal	Polys. show toxic granules
8-31			3,200	26	5	68	1				
9-4			500			100					A granulocytic picture.
9-20	53	2.88	2,300	16	6	76	1	1			
9-26	62	3.36	3,000	26	5	68	1				
9-31	70	3.39	4,050	24	12	63	1				
10-3	67	3.69	4,100	70	4	26					

months. Ecchymoses over the extremities had become apparent without known cause. His past history was noteworthy in that he had been told by another physician seven years before that his liver was enlarged.

On physical examination there was a large hard mass in the right upper quadrant. This was not tender and did not pulsate. Several soft enlarged lymph nodes were felt in the cervical, axillary and inguinal regions. The spleen was not enlarged.

His initial blood count revealed a hemoglobin content of 80 per cent, with 4 million red blood cells. There were 22,500 white cells per cu. mm., with 72 per cent lymphocytes, 15 per cent segment polymorphonuclear leucocytes, 5 per cent band forms, 3 per cent monocytes, 4 per cent eosinophiles and 1 per cent basophiles. There were 190,000 platelets per cu. mm. The successive blood

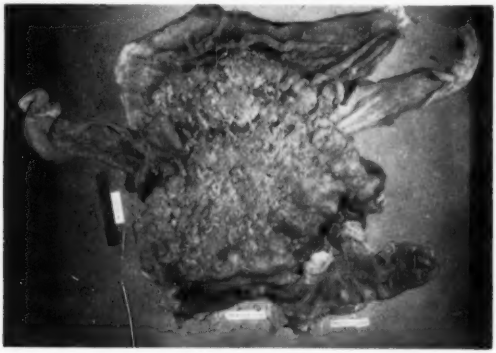

Fig. 2—Necropsy specimen of stomach. The entire cardia and *pars media* are involved in an extensive carcinoma.

counts are tabulated in Table I, and show a recession of the lymphocytosis of eight months.

His blood chemistry determinations, including urea nitrogen, total proteins, cholesterol, thymol turbidity and cephalin flocculation tests were all normal. His urine was clear. The blood Mazzini test was negative.

Gastric analysis revealed free hydrochloric acid. Gastric cytologic Papanicolaou examinations revealed no malignant cells. His stool was strongly positive for occult blood.

Bone marrow aspiration revealed infiltration with lymphocytes which were scattered in groups, aggregating about 30 per cent of the nucleated cells. No malignant cells were seen. Smears made by aspiration from an axillary lymph node (Fig. 3) showed mostly small mature lymphocytes with deeply staining lumpy nuclei and scant cytoplasm. These cells were of the "grumelee" type[4,5].

Also interspersed were a few large reticulum cells and some larger well-differentiated lymphocytes. A lymph node biopsy (Fig. 4) showed the cytoarchitecture to be obliterated by sheets of well stained small round cells with little cytoplasm and deeply stained nuclei. These cells extended into the capsule and surrounding fat lobules. It was the opinion of the pathologist that the picture was compatible with leukemic lymphadenosis.

Radiologic examination of the upper gastrointestinal tract showed normal passage of barium through the esophagus. At the cardioesophageal junction

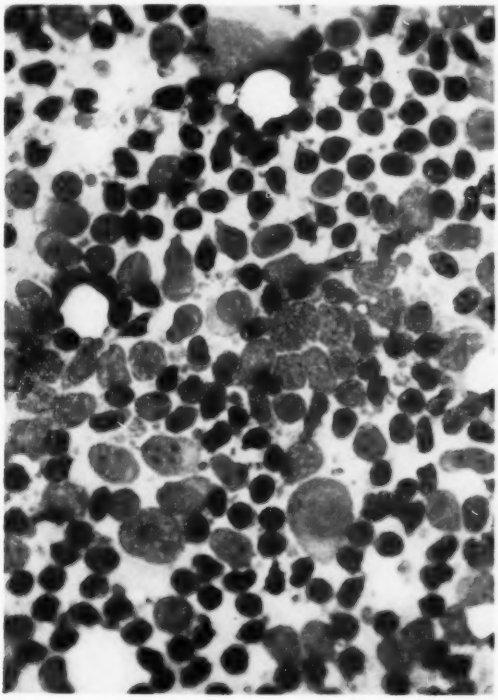

Fig. 3—Smear from axillary lymph node aspiration. Predominant are small deeply staining lymphocytes with checkerboard nuclei of the "grumelée" type. Several larger, pale staining lymphocytes are seen and an occasional reticulum cell. High power magnification (x1,200). Wright stain.

there was a slight hesitation, and the stream of barium projected over a prominence at the superior aspect of the lesser curvature. The stomach (Fig. 5) was of average size. Projecting into the lumen were many thickened rugal folds, some of which assumed a nodular appearance. The findings were believed compatible with leukemic infiltration of the stomach wall. The process at the

lesser curvature was difficult to identify, and it was believed that carcinoma could not be excluded in this region.

Further radiologic investigations, including chest and colon examinations and intravenous urography were all normal.

In view of the diagnosis of chronic lymphatic leukemia with gastric involvement, deep x-ray therapy was instituted over the stomach. An anterior and posterior field, each 10 x 15 cm., were given 200 r in air, twice over the anterior portal and three times over the posterior portal. The physical factors were 200 KV, 1 mm. cu., 1 mm. al. filtration, 50 cm. t.s.d. Treatment was started February 6, 1952 and concluded February 13, 1952. The response was rapid and most gratifying, with subsidence of gastrointestinal symptoms and marked diminution in the size of the mass in the right upper quadrant. The patient's sense of

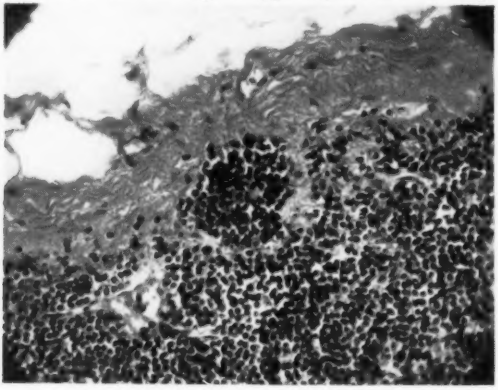

Fig. 4—Biopsy of axillary lymph node. Replacement of normal cytoarchitecture with small lymphocytes. Invasion of capsule (x400).

well-being improved. Roentgenogram of stomach (Feb. 25, 1952) showed little change (Fig. 6).

His leucocyte count fell to 4,900 within nine days after treatment was started. The differential count showed 30 per cent lymphocytes, 64 per cent neutrophiles, 6 per cent monocytes and 1 per cent eosinophiles. He was given two blood transfusions, and the count then was 5,200 with the same differential pattern.

About one month later he again complained of abdominal cramps and left upper quadrant pain. He passed a tarry stool together with bright red blood. Physical examination disclosed a mass in the right upper quadrant three finger-breadths below the costal margin. Marked tenderness and resistance was felt in the right upper abdomen. The spleen was not palpated. Diffuse lymphadenopathy was present. His blood count revealed a hemoglobin of 40 per cent with an erythrocyte count of 2.2 million. His white count was 7,000, with normal

differential. He was given several transfusions, and started on urethane gr. 1 daily for three weeks.

Re-examination of the upper gastrointestinal tract five weeks after the completion of his x-ray therapy revealed what appeared to be a recession in the thickened rugal folds (Fig. 7). Two months thereafter, a third gastrointestinal examination disclosed a very large mass lesion in the upper three-fourths of the stomach, with the antrum and duodenum uninvolved in the process (Fig. 8).

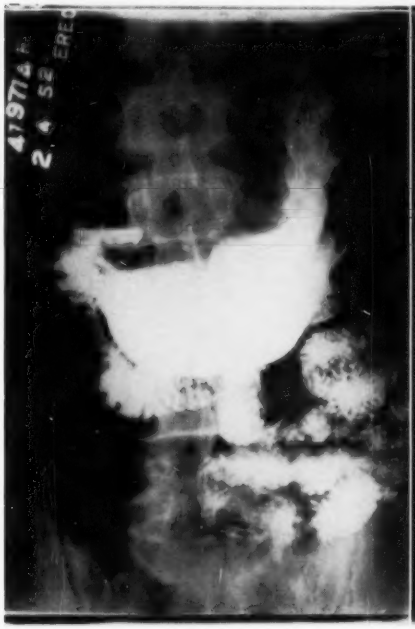

Fig. 5

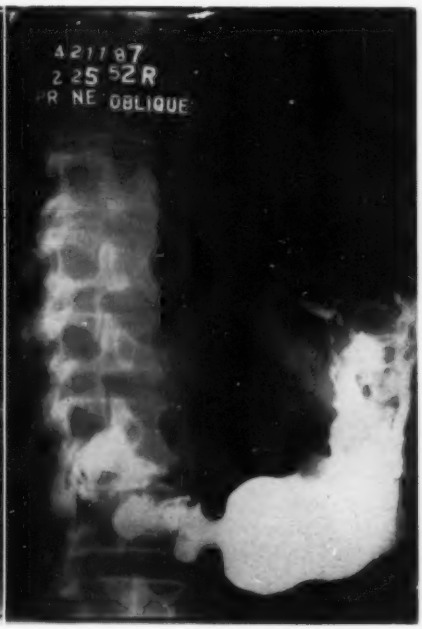

Fig. 6

Fig. 5—Roentgenogram of stomach before treatment.

Fig. 6—Roentgenogram of stomach two weeks after x-ray therapy. Scalloped irregularity of the walls of the lesser and greater curvatures of the upper half of the stomach. Note the large rugal fold in the middle.

Symptoms persisted, and on the advice of the hematologist 5 mg. of triethylene melamine was given every other day for three doses. The resistant feel in the left upper quadrant and the diffuse lymphadenopathy diminished, and the mass in the right upper quadrant became smaller. The patient seemed to feel better. On the tenth day of this regimen there was again a tarry stool with bright red blood. His leucocyte count fell to about 500, with a complete agranulocytosis. His white count increased gradually, and about six weeks later a normal differential count was obtained.

Nevertheless, the patient did poorly, developed bronchopneumonia and expired November 22, 1952.

At necropsy the stomach (Fig. 1) was firm, massive and dilated. The external surface was perforated at several points and adherent to the liver. The entire mucous surface was replaced by pink fungating papillary carcinoma (Fig. 2), which on microscopic examination proved to be mucinous adenocarcinoma. The regional lymph nodes showed metastatic carcinoma, but the

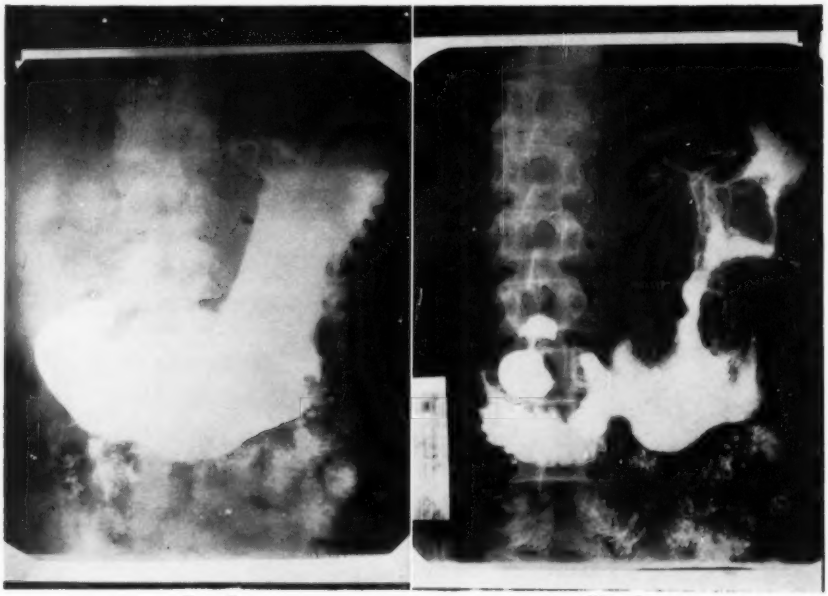

Fig. 7 Fig. 8

Fig. 7—Five weeks later, note lesser degree of scalloping of lateral walls of stomach.
Fig. 8—Nine weeks after x-ray treatment, note the masses in the upper three-fourths of the stomach are much larger.

retroperitoneal nodes presented chronic leukemic lymphadenosis. Metastases were present in the liver, which was also the site of portal cirrhosis, fatty degeneration and leukemic infiltration.

The spleen presented leukemic infiltration, extramedullary hematopoiesis and chronic perisplenitis. It was not enlarged. The bone marrow also showed lymphatic leukemic infiltration.

The immediate cause of death was lobar pneumonia of the left upper lobe with pleural effusion.

Comment

In the differential diagnosis of the blood picture of this patient the possibility of a leukemoid reaction was considered. Such changes may be seen with high peripheral white blood cell counts, with immature cells usually of the granulocytic type. Lymphatic leukemoid reactions, however, also have been reported[2,6,7]. In such cases no evidence of leukemia is seen at necropsy. In our case the postmortem changes confirmed the clinical diagnosis of lymphatic leukemia. The presence of leukemic infiltration of the gastric walls is rather uncommon, and when extensive is manifested as a rule by coarse, diffuse thickening of the rugal folds as seen in our case. A definite mass lesion such as was seen in the cardia in our patient, however, is not what may be anticipated from uncomplicated leukemia, and therefore raised the suspicion of a concomitant gastric malignancy. Watson[10] points out that specific leukemic infiltration of the stomach and bowel are uncommon in myelogenous leukemia, but may be extensive in lymphatic leukemia, particularly in cases with low total leucocyte counts. Machella[11] finds that leukemic infiltration of the stomach may give rise to clinical and roentgenologic characteristics of gastric carcinoma.

In some histologic respects our case resembled follicular lymphoblastoma in that there was a tendency to a follicular arrangement of the cells in the lymph node biopsy. There were no clear retracted areas around these follicle-like masses[8]. The predominant cell was a mature, well differentiated lymphocyte. While lymphatic leukemia and follicular lymphoblastoma are considered as closely related, and one condition has been observed to merge into the other, we believe that such was not the case on our patient[9].

The effect of the x-ray therapy, urethane and triethylene melamine on the peripheral blood count is difficult to assay. There is little doubt but that the spleen was included in the field of treatment for x-ray therapy, and the agranulocytic effects of urethane and TEM are well known. Nevertheless, it is difficult to ascribe the change in the leucocyte pattern during the course of the disease to these agents alone, and although we cannot give a specific answer it is felt that possibly the effects of inanition and cachexia consequent to the gastric carcinoma may have contributed to this interesting development.

Conclusion

A case of concomitant gastric carcinoma and lymphatic leukemia is presented. The clinical picture was of interest because of recession of the leukemic picture as the gastric malignancy advanced.

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EMPHYSEMATOUS GASTRITIS*

BERNARD FARFEL, M.D.

and

RALPH EICHHORN, M.D., F.A.C.G.

Houston, Texas

Emphysematous gastritis is a condition rarely encountered, and when encountered, perhaps unrecognized. A survey of the literature reports only five previous cases, the first being described by E. Fraenkel[1] in 1889. Others of course may be buried in the literature under other titles.

As will be developed later, this is the first case described that had an extensive coverage including repeated x-rays and other laboratory tests, gastroscopy, and laparotomy. The diagnosis was not made until late in the course of the disease.

Emphysematous gastritis is a form of gastritis manifested by the presence of a gas-producing microorganism situated between the *muscularis mucosa* and the submucosa of the stomach. In this condition, in contrast to the usual forms of gastritis, x-ray examination should be superior to gastroscopy as a means to determine the diagnosis.

The emphysematous process can be limited to one organ, in this case the stomach, as in similar instances it can be limited to the gallbladder, urinary bladder, or uterus. One should expect to find the condition more likely to exist in the presence of, or resulting from, a bacteremia due to a gas producing organism. It would appear logical to expect the occurrence of an emphysematous gastritis in the presence of an atrophic gastritis, particularly where diabetes or some debilitating disease already exists.

Fraenkel[1] reported a 35-year old patient who had attacks of severe abdominal pain, bloody vomitus, and diarrhea. At autopsy, rod-like organisms and masses of gas vesicles were found between the muscularis mucosa and the submucosa of the stomach.

Morton and Stabins[2] reported a 72-year old patient who was operated upon for a perforated duodenal ulcer. For five days the patient did fairly well, then took a turn for the worse. He died two days later, and at autopsy a phlegmonous gastritis due to B. Welchii was found. A necrotic area about the suture line suggested this point as a probable source of entry for the organism.

Weens[3] reported a 37-year old patient who developed emphysematous gastritis following the ingestion of concentrated hydrochloric acid in an at-

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tempted suicide. Three days later gastric lavage revealed the presence of B. Proteus. Sulfadiazine was given to combat infection. Three days later roentgen examination of the abdomen disclosed an emphysematous process involving the stomach. The patient's condition became worse the third week of his hospital stay and the blood culture showed A. Aerogenes. Penicillin was given. Five weeks after admission the gas formation in the stomach wall cleared. The patient succumbed five months later as a result of complications following contractures of the midportion of the stomach.

Welch and Jones[4] reported a 15-year old girl who developed what appeared at first to be an acute gastroenteritis with nausea, vomiting, and diarrhea. She became severely ill and was hospitalized. A film of the abdomen did not show any pathology. Six days later roentgen changes of emphysematous gastritis were noted. Three weeks later, after having received intensive penicillin therapy, the patient had recovered and the x-rays were clear. The exact organism which invaded the stomach wall is not known, although E. Coli, nonhemolytic streptococci, and staphylococcus aureus were found on culture of gastric contents obtained upon admission to the hospital. This patient was the first reported to recover.

Henry[5] reported a 1-month old male infant with diarrhea commencing shortly after birth. Blood culture disclosed *staphylococcus aureus*. One week later, after penicillin, fluids and plasma, there had been considerable improvement with cessation of diarrhea. One day later the child became acutely ill again. X-rays disclosed characteristic findings of emphysematous gastritis. The child died the same day. Autopsy disclosed innumerable bullae primarily. The bullae were found to be compressible, but no crepitus was felt. E. coli was grown from the stomach.

Case Report

A 76-year old white male, F.M., was admitted to the Medical Service of the Jefferson Davis Hospital on three occasions. The first admitting diagnoses were diabetes mellitus and possible intestinal obstruction. The chief complaint was obstipation which was relieved by breaking up a fecal impaction. He was in the hospital from December 6, 1953 to January 23, 1954.

During this stay he had a negative colon x-ray study. On December 16, 1953, December 23, 1953, and January 11, 1954 he had x-rays of the stomach. The report on all occasions was of food in the stomach.

The second admission was three months later on March 21, 1954 and he was discharged on May 31, 1954. The history this time was of diarrhea for a period of six weeks. Also, his diabetes was uncontrolled. On March 31 he again had x-rays of his stomach, and the report again was that the stomach contained food. It was suggested that he be returned for re-ray after aspiration of the

stomach contents. On April 28 the stomach was aspirated and x-rays repeated. This time it was felt that a filling defect was present along the greater curvature of the stomach.

On May 8 stomach x-rays were repeated. At this time the examiner was uncertain whether an intrinsic lesion was present or there were filling defects from retained food. The roentgenologist suggested gastroscopy. This was not done because of some evidence of cirrhosis and the possibility of rupture of varicose veins of the esophagus was considered.

It will be noted that this patient had now had six x-ray examinations of the stomach, twice after aspiration of the stomach contents.

Incidentally, chest x-rays and stool examinations were normal. During this admission some penicillin and gantrisin were administered empirically.

On May 24 an exploratory laparotomy was performed. The reason for laparotomy apparently was the confusing result of six upper gastrointestinal studies.

Upon opening the abdominal cavity, 1,500 c.c. of ascitic fluid was found. The stomach is described as appearing grossly normal. The stomach was palpated by the surgeon, who reported that it felt as if it contained a moderate amount of "mushy" material which appeared through the stomach wall to resemble barium in some areas. There was no evidence of a mass in the stomach and no evidence of any abnormality of the serosa. The stomach itself unfortunately was not entered. Examination of the colon and rectum was negative. The liver was small, contracted, and hobnailed. The gallbladder was not identified because of dense fibrous adhesions between the anterior surface of the first part of the duodenum and the gallbladder which probably represented the sealing-off of an old duodenal ulcer.

A normal appendix was removed. Liver biopsy confirmed the clinical diagnosis of portal cirrhosis. The man was discharged one week later.

The third admission occurred nine weeks later on August 8, 1954. The complaints noted included diarrhea of 12 weeks' duration and leg pains of five months' duration. The diarrhea was described as the passage of three to five large foul smelling stools a day. There was no blood noted. The stools consisted largely of mucus. The patient complained of weakness and loss of appetite. There was no nausea, vomiting or abdominal pain. No jaundice had appeared.

Past history included a fracture of the left hip in 1940, and the advice to take 10 units of NPH insulin and a restricted diet which was not followed very closely.

Essentially the physical findings on admission included the following:

Blood pressure—115/60, pulse rate 80 per minute, respirations 20, and temperature orally—98°F. The patient appeared chronically ill with signs of weight loss and malnutrition. The skin was dry and scaly. There was evidence of early cataract formation and all teeth were absent. No lymphadenopathy was present. Ears were normal; the nose negative. Tongue was moist and protruded in midline. Tonsils were absent. Thyroid was not enlarged. Heart sounds were of fair quality. The heart was not enlarged. All pulses were palpable, irregular and a pulse deficit of 10 plus was noted. No murmurs were found on this examination. A_2 was greater than P_2. Lungs were clear to percussion and auscultation. The abdomen was protuberant with a lower well-healed midline scar. Liver was palpable but not enlarged. Bowel sounds were normal. Rectal examination was negative for masses. Prostate was of normal size and consistency. Extremities showed no edema, varicosities, or ulcers. Reflexes were normal, equal and active.

At this time the chest x-rays were normal. X-rays of the stomach again showed the same findings previously noted. Gastric analysis after histamine showed no free acid. Serology was negative. An iodine uptake study was low. A small bowel series was normal.

On September 23 this patient was presented at medical conference. It was at this conference that the true nature of the diagnosis was disclosed.

On September 28 gastroscopy was performed. The pylorus was not visualized. There was minimal peristalsis. The stomach walls appeared thin, grey, and atrophic, and the vessels appeared accentuated. The rugae had disappeared. None were seen except in the cardia where a few irregular folds remained. There were strings of yellowish-white mucus on the gastric mucosa. No ulceration, hemorrhage nor foreign body was seen. Gastroscopic diagnosis was given as atrophic gastritis.

Several urine cultures which were done on October 18 and October 25 showed the presence of aerorobacter and pseudomonas. These cultures were done when the urine was found to contain 15-20 RBC/HPF. The urinary sediment was loaded with WBC and there were a few casts present. The specific gravity was 1.024 and 4+ albumen was present. Hemoglobin determinations during this period averaged 8.5 gm. A stool examination on August 14 was negative for parasites, ova, cysts, occult blood or fat. The stool examination was repeated on five occasions with the same findings. The red blood count averaged 4,100,000. Hematocrit was 33 per cent. The white blood count was 9,500. The differential examination was normal. The red cells were normocytic and displayed hypochromia. The corrected sedimentation rate was 10 mm/hr. Other findings included a blood sodium of 136 mg. per cent, potassium—3.3 mg. per cent, plasma chlorides—108 mEq. per liter, a serum amylase of 78 and 100. On August 7 the total proteins were 6.2, the albumen being 3.0. Acid and alkaline phosphatase were normal. The serology was negative. The blood urea

nitrogen was 15. Thymol turbidity was 10. A fasting glucose on August 5 was 450 mg. per cent. The bromsulfalein showed 10 per cent dye retention on August 5. The temperature from the date of admission to the 29th of August was normal. For two days it ranged from 100°F to 102°F and returned to normal and remained so until the date of discharge on October 26. A bone marrow study on August 10 revealed no abnormality.

Therapy during this time was largely symptomatic including multivitamin capsules, diabetic diet, NPH insulin, and a display of many medications, including pyridium, sulfasuxadine, folic acid, chloroquine, gantrisin, procaine penicillin, dilute hydrochloric acid, digitalis, lipomul, resion and achromycin. Achromycin was given the day of discharge only.

To summarize, the chemotherapy and antibiotic therapy prior to the date of conference included pyridium for one month, sulfasuxadine for one week, chloroquine for two weeks, gantrisin for three days, 600,000 units of procaine penicillin daily for eighteen days, gantrisin again for the two weeks prior to his discharge on October 26.

The two organisms under suspicion are B. Proteus and *Aerobacter aerogenes*. Bacillus proteus is an aerobic facultative anaerobe which develops fairly well in urine. One suspects that it reaches the stomach through the blood stream. *Aerobacter aerogenes* is normally found in the feces. It has been isolated commonly from infections of the urinary tract, peritoneum, liver and gallbladder. We have no proof that these organisms actually invaded the stomach wall. No biopsy of the stomach wall was taken during the laparotomy. We believe, however, there are several conclusions one can draw from a review of this case and those that were described earlier.

The roentgen picture of emphysematous gastritis resembles a stomach containing retained food and secretion. The rugal pattern is bizarre and all normal rugal pattern is destroyed throughout the entire stomach. The pattern is inconstant and changes on repeated examination. The picture is the result of emphysematous blebs in the stomach wall. This picture may be differentiated from retained secretion if one is certain that no secretions are retained and if the stomach is lavaged and emptied prior to filming. The remainder of the gastrointestinal examination remains normal.

One should suspect the diagnosis of emphysematous gastritis in the presence of an unexplained diarrhea, particularly in a situation where any type of gastritis may ordinarily be present. Diarrhea seems most likely to be the presenting complaint. One must conclude from this and previous reports that the diagnosis can be best made and perhaps only be made as a roentgenological diagnosis and/or at exploration. This is the second case reported to have recovered. Whether complete recovery followed is questionable since no follow-up is available. It would seem, however, that having once recognized this

condition and the organisms most likely to be associated with an infection of this type, one could employ the proper therapeutic agent to bring about improvement and recovery. Since this is one of a very few reported cases, including the first in 1889, one must consider the condition as a very rare one or, as is very likely, a seldom recognized one. I believe that this report may bring to mind other similar undiagnosed cases of emphysematous gastritis. It would seem logical to expect that the incidence would be much higher than is apparent from the few cases reported in the literature to date. Several x-rays have been included to demonstrate the unusual roentgen picture which this entity presents.

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NAUSEA AND VOMITING, WITHOUT ABDOMINAL PAIN, DUE TO GIARDIASIS

MICHAEL WEINGARTEN, M.D., F.A.C.G.
New York, N. Y.
and
JESSE J. SERWER, M.D.
Glendale, N. Y.

The object of this report is to present a group of six patients, in whom recurrent episodes of vomiting, unattended by any abdominal pain and without anorexia or weight loss, were associated with an infestation by *Giardia lamblia*, and whose symptoms were eliminated by eradication of the parasite by treatment with atabrine. Although clinical articles detailing the symptoms of giardial infections have appeared in which nausea and vomiting are mentioned, their occurrence as isolated symptoms has been mentioned only once previously in a report by us of a single case in 1945[1]. Since then, when confronted by a similar syndrome, we have had a careful examination of a warm, purged stool performed by a competent parasitologist, and are now able to add five additional cases, three adults and two children.

Every author who reports cases of giardial infestation finds it necessary to enter the debate as to the pathogenicity of this protozoan inhabitant of the duodenum and upper small intestine of man. Despite numerous clinical reports in the literature of giardiasis with clinical manifestations which were relieved by the eradication of the parasite, its pathogenic role is generally unrecognized to the extent that *Giardia lamblia* is not even mentioned in recent editions of standard texts in internal medicine. There are, to be sure, reports which deny any role to *Giardia lamblia* in the production of symptoms. In this connection, Hartman and Kyser[2] in an excellent review of the topic, state: "Clinical articles on the subject of giardiasis usually announce that giardiasis does not produce symptoms. The author of such an article then proceeds to present clinical evidence which demonstrates that giardiasis produced the symptoms in his cases". Until 1937, when Galli-Valerio discovered that atabrine was a specific against *Giardia*, there was no effective therapeutic agent which made it possible to evaluate the relationship of symptoms to the presence of *Giardia* in the intestinal tract. Most of the reports casting doubt on the pathogenic role of *Giardia lamblia* antedate 1937, or else atabrine was not employed, as in a report published in 1946[3], which denies the pathogenicity of *Giardia* on the basis of treat-

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From the Gastroenterological Division, Department of Medicine, Beth Israel Hospital, New York, N. Y.

ment with carbarsone. Belding[4] states the arguments in favor of the pathogenicity of *Giardia lamblia* as follows: 1. ulcerative lesions in the presence of numerous parasites at autopsy, 2. the occurrence of fulminating cases, 3. its association with a syndrome of diarrhea, steatorrhea, cachexia and biliary disease, 4. interference with the normal absorption of fat and Vitamin A, (corrected by treatment[5]) and 5. the frequent disappearance of symptoms after removal of the parasite.

More closely related to the symptom of vomiting in the patients in this presentation are reports of: 1. catarrhal inflammation of the duodenum[6], 2. extensive denudation of the upper small intestine[7], and 3. the radiological demonstration of functional and anatomical changes in the pylorus and duodenum in 50 to 73 per cent of patients with giardiasis[8,9].

Case Reports

Case 1:—D. G., a 31-year old married, white female, was seen November 10, 1942. She had given birth to a living child in November 1938, after a pregnancy which was marked by persistent vomiting from the fourth to the eighth month. This vomiting was considered to be due to the pregnant state. In May 1939, however, six months after delivery, she again commenced to vomit after every meal without experiencing any pain. This lasted for three months and then ceased. In June 1942, vomiting after every meal recurred, again without any abdominal pain, but she experienced occasional heartburn. The vomitus consisted of undigested food, always a fraction of what she had eaten, and there was no loss of weight. There was no blood in the vomitus. The previous medical and surgical histories were negative. She had consulted several gastroenterologists, and repeated roentgenographic studies of her gastrointestinal tract had been made with negative results. Her vomiting was considered to be on a psychoneurotic basis.

Except for the obesity, there were no abnormal physical findings. Neurological examination was entirely normal and all routine laboratory studies were negative. Gastrointestinal x-rays, proctoscopy and barium enema were normal. Cholecystography revealed a moderately large gallbladder, which failed to contract after a fatty meal. There were no calculi. Because of the persistence of the symptoms, and failure of the gallbladder to contract, duodenal intubation for drainage of the gallbladder was performed. All of the specimens obtained, A, B, and C bile, swarmed with motile *Giardia lamblia*. Atabrine 0.1 gm. was prescribed to be taken three times daily for five days. The vomiting ceased after she had taken nine tablets. Two weeks later, no *Giardia* were found on duodenal intubation. Thirteen years have now elapsed, and there has been no recurrence of vomiting.

Case 2:—The next case encountered was that of a 10-year old white boy, S. L., who was referred by a pediatrician in April 1949, because for a few

months he had vomited after breakfast on week-days before going to school. He was an intelligent, well-behaved youngster who enjoyed being at school, and protested whenever an illness made it necessary for him to absent himself. Nevertheless, his failure to vomit on Saturdays and Sundays raised the question of some psychological factor. There was no history of abdominal pain, and physical examination and routine laboratory tests were entirely negative. A gastrointestinal x-ray study revealed a moderate, intermittent spasm of the second portion of the duodenum. Warm, purged stools were examined for ova and parasites by Dr. Howard B. Shookhoff and were found to be negative. After a few weeks, the vomiting ceased spontaneously. Six months later, he was again referred by the pediatrician because his morning vomiting had recurred and he was now vomiting every day of the week, including Saturdays and Sundays. Radiological studies again revealed spasm of the descending duodenum. A purged stool was again examined and was now reported to show the presence of trophozoites and cysts of *Giardia lamblia*. Atabrine was administered, and the vomiting promptly ceased and has not recurred to date.

Case 3:—J. E., an unmarried white female, age 61 years, was seen in November 1949. For ten years, she had had recurrent episodes of nausea and vomiting after meals. Occasionally, she experienced mid-abdominal pain after the effort of vomiting. Three years previously, a laparotomy was performed at another hospital for a gastric polyp, diagnosed by x-ray, but not found at exploration. A normal appendix was removed. She was often awakened at night with nausea and then would vomit all night. In the past three years, she had lost about 17 pounds, although her appetite was good. There was considerable heartburn at all times. On physical examination, there was a right rectus scar, but no other abnormalities. Gastrointestinal x-rays revealed moderate pylorospasm and hypertrophied gastric rugae, but no other evidence of gastrointestinal pathology. A warm, purged stool was examined and reported to show an occasional cyst of *Giardia lamblia*. Two days after commencing atabrine, her vomiting ceased, though the nausea persisted. Heartburn was less. Two months later, she reported complete freedom from the previous complaints.

Case 4:—M. K., age 29 years, married, the daughter of a hospital employee, was referred in March 1950, with a history that four years previously she began to have episodes of nausea with occasional vomiting, which often was induced, but was not always effective in relieving the nausea, which at times lasted all day. Food ingested while she was nauseous did not increase her distress, and in the free intervals her appetite was good, so that while her weight fluctuated, there had been no weight loss. There had never been any abdominal pain, but she had pyrosis at times. Physical examination and routine laboratory tests were completely normal, and gastrointestinal x-rays revealed normal findings. A purged stool was examined and the presence of many motile trophozoites and cysts of *Giardia lamblia* was reported. Atabrine

was administered with complete relief of symptoms for nine months. In January 1951, she had a recurrence of her symptoms for several days. Another course of atabrine was administered. She has remained symptom-free since then.

Case 5:—N. Z., a female, aged 11 years, was seen in January 1955. Two months previously, she began to experience nausea and vomiting which lasted for three days. At the onset there was no pain, but after a prolonged period of retching, nausea and vomiting, the child experienced superficial epigastric discomfort, attributed to the effort of vomiting. She had been admitted to a hospital where all laboratory studies performed, including x-ray studies of the gastrointestinal tract, were negative. The symptoms were attributed to a psychic trauma which the child had experienced two weeks before the onset. She continued to have these episodes of nausea and vomiting once or twice a week. Her appetite was good and there was no weight loss. She was a well-developed and well-nourished child, whose physical examination was entirely negative. Gastrointestinal radiographic studies were negative. A warm, purged stool was examined by the Tropical Disease Diagnostic Service of the New York City Department of Health, and was found to contain trophozoites and cysts of *Giardia lamblia*. Atabrine 0.1 gm. was administered three times daily for five days. The symptoms promptly ceased and have not recurred.

Case 6:—L. B., a white male, aged 52 years, was seen by the junior author in May 1952, because of severe and prolonged nausea and weakness. Six months previously he had begun to experience attacks of nausea which occurred daily, gradually increased in severity and number and which were without relationship to food. In the previous few weeks nausea had reached such a degree that vomiting seemed imminent, but he had not vomited. Accompanying the nausea from its original onset the patient had noted a mild and occasional weakness. This had increased so that it was present every day at various times during the day. The patient was well-nourished. On physical examination, there was slight but questionable tenderness to the right of the umbilicus but no other abnormalities. Routine laboratory studies and gastrointestinal x-ray studies were normal. Examination of a freshly purged stool revealed large numbers of trophozoites and cysts of *Giardia lamblia*. A course of atabrine was administered. Four weeks later he was completely free of his symptoms of nausea and weakness. Examination of freshly purged stools several months later did not show the presence of cysts or trophozoites of Giardia. The symptoms have not recurred.

Comment

A single course of atabrine, 0.1 gm. given three times daily for five days, will cure 94 per cent of patients with giardiasis. Another six per cent require a second course, after which the infestation is nearly always eliminated. The

availability of such an effective agent should end the debate as to the pathogenicity of *Giardia lamblia* in those cases where thorough examination reveals it to be the only cause for the symptoms encountered.

In the series of cases reported above, four were adults and two were children. This is because the authors' practices are almost entirely confined to adults with an occasional reference of a child by a pediatrician. Generally, *Giardia* is much more prevalent in children than in adults, which has led some to believe that in many instances there may be spontaneous elimination of the parasite.

Patients with severe symptomatology with giardial infestations are reported especially by European authors. The role of *Giardia lamblia* in biliary tract disease is not established. Severe diarrhea, steatorrhea, abdominal pain and distention, anemia and retarded development in children are described. The senior author has seen five cases of mild diarrhea and three of persistent heartburn, which are not included in this report, who were cured by the elimination of *Giardia lamblia* from the intestinal tract. One patient, a very successful attorney, with persistent, severe postprandial pyrosis for 15 years is perhaps worthy of special mention. He had consulted many gastroenterologists and internists, and always after negative gastrointestinal x-ray studies was told that his heartburn was on a psychosomatic basis. Examination of his stool revealed many motile *Giardia*. After a course of atabrine, he was promptly relieved of his heartburn, which has not recurred in four years.

Given a patient with abdominal complaints and negative physical, routine laboratory and radiological examinations, the tendency to ascribe the symptoms to a psychosomatic state is great. To do so, without performing an examination of warm, purged stools, can lead to serious error and failure to cure the patient. This is true both in chronic amebiasis[10] and in giardiasis. The symptoms of three of the patients reported above easily lent themselves to the interpretation of being of psychosomatic origin.

That a giardial infestation may cause nausea and vomiting without abdominal pain is not surprising in view of its known localization in the duodenum and upper intestinal tract and the report of catarrhal inflammation of the duodenum and of radiological abnormalities, notably spasm of the duodenum.

Summary

Six cases are reported, four adults and two children, who had recurrent episodes of nausea and vomiting over long periods of time without experiencing any abdominal pain. In one patient, duodenal spasm was found on repeated x-rays of the gastrointestinal tract. All had a *Giardia lamblia* infestation, and were permanently cured by the administration of atabrine.

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SPECIAL GASTROENTEROLOGICAL DIAGNOSTIC PROCEDURES

J. ALFRED RIDER, M.D., Ph.D.
LEO VAN DER REIS, M.D.
and
JENNIE LEE, M.D.
San Francisco, Calif.

The medical subspecialty of gastroenterology seems to lend itself to a wide variety of unique diagnostic methods and procedures. It is the purpose of this paper to review the current procedures by describing the various types of equipment available, stressing the indications, contraindications and scope of their use. These procedures are not meant to take the place of an accurate history and physical examination, nor are they designed to compete with diagnostic x-ray and fluoroscopic examination. They do, however, complement these more routine methods of examination and thereby improve diagnostic accuracy. Although liver biopsy and peritoneoscopy are part of these special procedures, because of lack of space they will not be discussed.

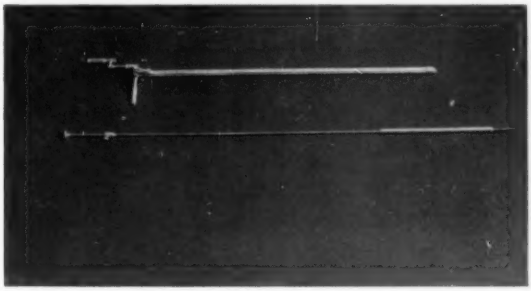

Fig. 1—Eder-Hufford flexi-rigid esophagoscope.

Esophagoscopy

This is a relatively old procedure and has usually been carried out by otorhinolaryngologists, endoscopists and thoracic surgeons. The most popular instrument was the hollow, rigid Jackson esophagoscope. It gave excellent visibility and could be used to diagnose abnormalities in the mucosa of the esophagus, strictures, tumors, carcinoma and esophageal varices. It was easy to biopsy the esophageal mucosa through this instrument. By using the esophagoscope and with biopsy and microscopic examination of the tissue, the

From the Gastrointestinal Clinic, Department of Medicine, University of California School of Medicine, San Francisco.

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diagnostic accuracy approached 100 per cent; at times, however, a stricture with a suspected lesion distally could not be seen or biopsied.

A more serious drawback, however, was the fact that a great deal of training and skill was required to pass the rigid esophagoscope through the pharynx and down the esophagus without perforating this most delicate section of the gastrointestinal tract. Even in the hands of experts occasionally perforation with subsequent serious or even fatal mediastinitis occurred.

To improve the safety of this procedure several flexible esophagoscopes have been developed[3,15]. We prefer to use the Eder-Hufford "flexi-rigid" esophagoscope[6] (Fig. 1). This instrument permits full visibility, can be used with biopsy forceps, and is relatively simple to introduce into the esophagus; the technic is almost identical with that used for gastroscopy. This instrument consists essentially of a standard Jackson-type esophagoscope which is fitted with a flexible stainless steel spiral obturator tipped with a flexible pointed rubber finger. The obturator can be adjusted to protrude as much as 6 inches beyond the open end of the scope. When the esophagoscope is passed to the

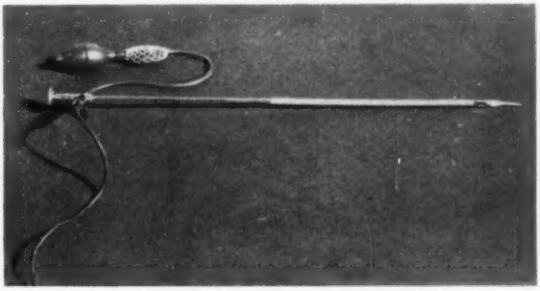

Fig. 2—Cameron-Omniangle gastroscope.

desired depth the flexible obturator is withdrawn, allowing examination through the rigid, hollow illuminated tube. This instrument retains the advantages of the rigid Jackson esophagoscope for clear vision and for biopsy purposes, but is safer and easier to use. It is well suited for the great majority of esophagoscopies, with the exception of high-lying extrinsic or intrinsic esophageal lesions where an esophagoscope should be introduced under direct vision at all times. Other contraindications are fever, severe cardiac disease, dyspnea, aneurysm of the aorta, extreme debility and lack of cooperation on the part of the patient.

The procedure is indicated for all lesions of the esophagus, either suspected or demonstrated by x-ray examination, including stricture, cardiospasm, tumors, carcinoma, hiatus hernia, esophagitis and esophageal varices.

Gastroscopy

The first examination of the stomach with a gastroscope was performed by Kussmaul[8] in 1868. It was not until 1932, however, that Schindler and Wolf[16]

developed a flexible, optically perfect gastroscope which made gastroscopy a safe and acceptable diagnostic procedure. This instrument, with little modification, is still the most widely used of all those available. In contrast to the esophagoscope, the gastroscope is not hollow, but consists of a central core made up of a series of mirrors placed in such a manner that bending of the instrument in the esophagus or stomach will not distort the image.

Although several very good instruments are commercially available, we prefer the flexible Cameron-Omniangle gastroscope (Fig. 2) because of its small diameter, light weight, ease of introduction, and because of the wide field of vision which is obtained, without moving the instrument, through the use of the built-in tilting mirror. The Eder-Chamberlain gastroscope, with an adjustable tip angulated from the ocular or proximal end, merits further investigation.

Gastroscopy is of great importance for confirming an x-ray diagnosis or for establishing the diagnosis of suspected lesions. It is of value in helping to

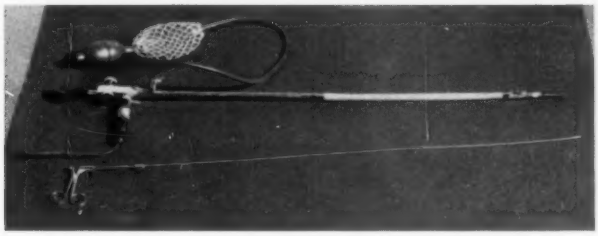

Fig. 3—Benedict operating gastroscope with forceps.

determine whether a gastric ulcer is benign or malignant and for following the healing course of a gastric ulcer. Lesions may be detected which were either not suspected or were not seen on x-ray examination of the stomach. Finally, it is the only reliable method for diagnosing gastritis.

That gastroscopy and x-ray are complementary, not competitive methods can be seen from the results obtained in 91 cases of gastric carcinoma reported by Schindler[17]. About 6 per cent of the lesions were not discovered by gastroscopic examination, and about 7 per cent were misdiagnosed. In approximately 27 per cent of the cases examined by x-ray, the lesion was either misdiagnosed or missed completely. By combining both methods the correct diagnosis was made in about 92 per cent of the cases. In a more recent article Klotz et al[7] found that in 410 patients with abnormal stomachs, 30 per cent were not diagnosed by x-ray examination, and 29 per cent were not diagnosed by gastroscopy. A combination of both methods reduced the diagnostic inaccuracy to 10.7 per cent. In only one case was the lesion completely overlooked, and in only 6 per cent was malignancy not diagnosed.

It is important to stress that whereas most of the inflated stomach is visible through the gastroscope, there are three main "blind areas": 1. The area of the lesser curvature of the antrum, 2. the lower pole of the greater curvature, and 3. the posterior wall which is hidden by the width of the gastroscope.

The indications for gastroscopy are as follows: 1. Lesions of the stomach seen or suspected on roentgen examination, 2. cases of upper abdominal discomfort in which x-ray examination shows no abnormality, but in which there is reason to suspect organic disease, 3. unexplained instances of hematemesis and/or melena, 4. pernicious anemia, because of its frequent association with polyps and carcinoma of the stomach, 5. patients who develop gastrointestinal symptoms following gastrectomy or gastroenterostomy, including those with stomal ulcers, and 6. hiatus hernia.

The contraindications to gastroscopy are: 1. Noncooperation on the patient's part unless general anesthesia is employed, 2. any obstruction of the esophagus or unusual angulation, such as that produced by marked kyphosis

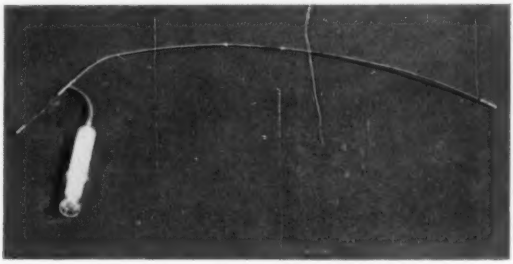

Fig. 4—Wood's suction biopsy tube.

or scoliosis, 3. aneurysm of the aorta, 4. septic oral disease, 5. severe cardiac disease or pronounced dyspnea. In addition, caution should be used when an esophageal diverticulum or cardiospasm is present.

Gastroscopic Biopsy

Although a biopsy could be obtained through the earliest rigid gastroscopes, it was not until the development of the Benedict Operating Gastroscope[2] (Fig. 3) that this procedure became widely used. Although this instrument is more awkward to use than the standard gastroscopes, it is possible to obtain a biopsy of a gastric lesion under direct visualization by using the attached biopsy forceps. For lesions favorably placed and in which the biopsy is successful, an unequivocably positive diagnosis can be made. The indications and contraindications are similar to those for the ordinary gastroscope.

Wood[21] has developed a flexible suction biopsy tube (Fig. 4) which is much simpler to use; however, since the specimens are obtained blindly, it is

usually not of value except where there is a diffuse lesion of the stomach. It may be more important as a research tool to study the gastric mucosa and its general response to various drugs or to irradiation. This ingenious flexible instrument consists of a hollow, coiled spring wire with an outer plastic cover. The distal end has a biopsy capsule with a small hole in its side. When suction is applied to the proximal end of the tube a small piece of mucosa is pulled into the lumen of the biopsy capsule. This piece is then excised by an internal knife which is forcibly drawn across the orifice of the biopsy capsule by means of an attached wire.

Tomenius[18] has developed a suction biopsy tube which is attached to a flexible Wolf-Schindler gastroscope. It is only possible to see the exact site of biopsy just after the procedure; it is impossible to see it while the specimen is being removed. The suction biopsy technic would be highly effective if true

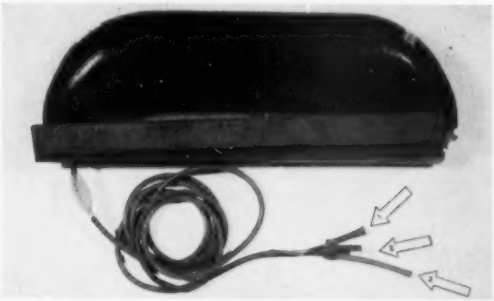

Fig. 5—Permanent steel magnet with magnetically tipped 3-lumen tube. 1—lumen for inflating rubber balloon. 2—lumen for duodenal drainage. 3—lumen for gastric drainage.

visual control could be developed. The Tomenius scope has been a great advance in this direction.

Proctosigmoidoscopy

This is an old, simple and accurate method for diagnosing lesions of the rectum and sigmoid to a distance as high as 30 cm. above the anus. Numerous excellent instruments are available; all consist essentially of a hollow, illuminated, rigid tube through which excellent visualization is obtained and through which biopsy is relatively simple. That this examination should be included as part of a routine general physical examination can be seen from the following data. In a recent study of 7,487 routine gastrointestinal clinic patients, 401 cases of polyp of the rectum or colon were found, an incidence of 5.4 per cent; of these 92.8 per cent were diagnosed by proctosigmoidoscopy[12]. The incidence of carcinoma of the colon and rectum in 7,086 patients without polyps was 2.1 per cent, whereas the incidence of carcinoma in the 401 patients with polyps was 10.7 per cent. Furthermore, it is important to stress that at least 75 per cent of all carcinomas of the colon and rectum are visible by proctosigmoidoscopy.

Gastric Analysis

As performed in our clinic, the technic consists of having the the patient swallow a Rehfuss tube. The gastric contents are then aspirated continually for one hour, but are divided into four 15-minute specimens. If no free acid is present, then an analogue of histamine called Histalog® (50 mg.) is given by hypodermic injections, and specimens are collected for another hour. Gastric analysis is valuable for the following reasons: 1. Since acid levels tend to be higher in patients with duodenal ulcers, this test can be used as confirmatory

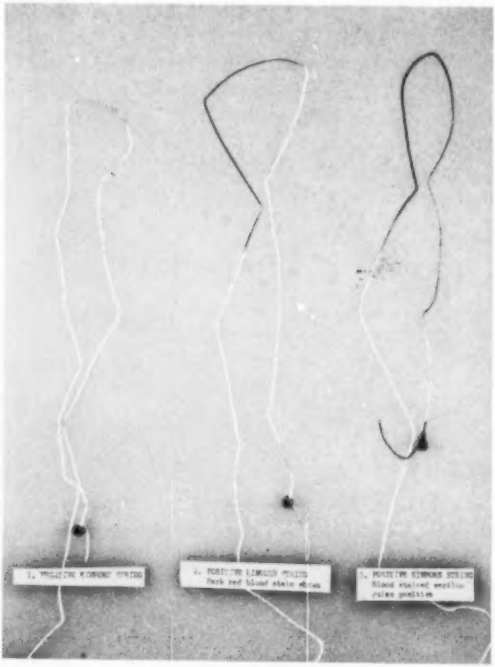

Fig. 6—Positive and negative Einhorn string tests. 1—negative. 2—positive, showing dark red blood stain. 3—positive, confirmed by guaiac test for occult blood.

evidence for a duodenal ulcer. 2. For practical purposes a duodenal ulcer or benign gastric ulcer is never present in a patient who has no free acid after three separate gastric analyses with histamine or Histalog. 3. The absence of free acid is one of the criteria for the diagnosis of pernicious anemia.

Duodenal Drainage

By introducing a Levin tube into the duodenum, it is possible to aspirate the duodenal contents, which can then be analyzed for the presence of pus cells, red blood cells, bacteria, crystals, bile and pancreatic enzymes.

Duodenal drainage is not new, but it is not done as frequently as it should be because it is often difficult to pass the tube into the duodenum, and because subsequent examination of the duodenal contents is time-consuming. Also, special laboratory facilities are usually required for a complete study. This procedure, however, may enable us to diagnose pancreatic disease earlier and more accurately, particularly carcinoma of the pancreas, which is almost invariably diagnosed when it is too late. It is also of value in diagnosing biliary tract disease, especially where infection is present.

Recently, a permanent steel magnet has been developed which facilitates rapid placing of a magnetically tipped 3-lumen tube into the duodenum and decreases the time necessary for the procedure (Fig. 5). Our own experience has confirmed the usefulness of this magnet.

Einhorn String Test

This simple test[4,5] was devised by Einhorn for the purpose of detecting and localizing bleeding from the upper gastrointestinal tract. The materials consist of a white silk thread (English braided silk No. 5) 36 inches in length and a small lead shot or "duodenal bucket" which is tied to the distal end of the string (Fig. 6). Knots are tied in the thread 22 inches and 32 inches from the shot.

The patient is not allowed any colored food or liquids the day of the test. Two hours after supper the patient swallows the string until the first knot is at the teeth. One hour later the string is swallowed to the second knot; the string is then taped securely to the face. The next morning just before breakfast the string is removed. In some cases x-ray of the abdomen will aid in localizing the end of the string. After it is withdrawn, the string is examined grossly for the presence of bile and blood. The presence of blood can be confirmed by either the benzidine or guaiac test.

The method of interpretation is as follows: The distance of the blood stain from the knot at the teeth indicates the site of bleeding. The distance from the teeth to the pylorus averages 22 inches. Esophageal bleeding stains the first 12 inches. A stain at 12 to 15 inches suggests bleeding at or near the cardia. A stain at 14 to 22 inches indicates gastric bleeding. The "bucket" or shot usually passes into the duodenum, and bile stains will appear on the last 10 inches. The presence of blood beyond 22 inches indicates duodenal bleeding. It may be necessary to repeat the test, especially if the hemorrhage has ceased at the time of the examination.

This simple and inexpensive test may accurately localize a bleeding area when x-ray and gastroscopic results are negative. It does not, however, give any clue as to the type of lesion.

The following case report indicates the usefulness of the string test: A 46-year old white man was admitted to the hospital because of weakness, tachycardia, recurrent melena and anemia. The past history was significant in that approximately one year previously he had undergone a subtotal gastric resection for a chronic duodenal ulcer and recurrent bleeding.

One month prior to his present admission to the hospital, his hemoglobin was 4.7 gm. per cent. After four blood transfusions the hemoglobin rose to 10.6 gm. per cent. The day of entry into the hospital the hemoglobin was 7.4 gm. per cent. The feces were tarry and showed 4 plus occult blood. A gastrointestinal x-ray examination revealed a well-functioning gastroenterostomy and no evidence of a stomal ulcer. Results of a pneumocolon and barium enema were reported to show no disease. The Einhorn string test revealed a blood stain about 4 inches long at a distance of 18½ inches from the teeth, which placed the site of bleeding at the stoma. This was confirmed by gastroscopy, which demonstrated a hemorrhagic area approximately 2 cm. in diameter in the depth of a large rugal fold on the anterior wall near the greater curvature of the stomach adjacent to the stoma. The findings were consistent with a shallow gastric ulcer.

A modified medical ulcer regimen was instituted. A second gastroscopy about 6 weeks later revealed no evidence of the previous ulcer. The hemoglobin was within normal limits, and the feces contained no occult blood.

It is of interest that this patient did not have any symptoms of an ulcer, even before treatment. The x-ray examination showed no abnormalities, but the string test localized the site of bleeding, which was then confirmed by gastroscopy.

Occult Blood in Feces

The determination of occult blood in the feces by benzidine, guaiac or orthotolidine method (Fecatest®)[13] is very simple. This test is important because the presence of chemical blood in the feces of patients on a red meat-free diet who are not swallowing blood from the nose, mouth or lung indicates a bleeding lesion in the gastrointestinal tract. This may be the only test to suggest a carcinoma or a bleeding peptic ulcer.

Exfoliative Cytology

Exfoliative cytology has been applied for many years as a diagnostic aid in gastroenterology. During recent years exfoliative cytology of the gastrointestinal tract has become more reliable and useful, especially through the efforts of Papanicolaou[11] and Meigs[10]. As a diagnostic procedure it rates favorably in accuracy with x-ray and endoscopy. Traut et al[19] reported that a possible accuracy of 85 per cent could be obtained by this procedure. Wisseman et al[20] reported on a series of 110 cases in which the cytological method was used to diagnose cancer of the rectum and lower colon. They achieved an accuracy of

76 per cent. Bader and Papanicolaou[1] concluded that, in their experience, cytology is dependable as a laboratory procedure in the diagnosis of malignancies of the lower intestinal tract. Rubin[14] reported an accuracy of 91 per cent in 216 proved lesions of the esophagus, stomach, pancreas and colon.

The diagnostic accuracy depends to a great extent upon the technic employed to collect the cells and tissue particles which are exfoliated. It is also necessary to keep the digestion of the cells to a minimum, as well as to eliminate food particles and debris. The interpretation of the specimen by a competent cytologist is, of course, indispensable.

The patient is given a liquid diet the evening prior to the examination. If evidence of obstruction is present, overnight suction should be used.

The technic is as follows: A rubber tube, such as a Miller-Abbott tube, is introduced through the mouth to the level of the suspected lesion. (We do not believe that the abrasive balloon or bag improves the accuracy.) This area is then washed for 10 to 15 minutes with 250 to 500 c.c. of a buffer solution containing papain, or preferably chymotrypsin. At the end of this period the fluid is aspirated and centrifuged immediately in order to shorten the time during which the enzyme can act on the exfoliated cells. Immediately after centrifugation the cells are fixed. After fixation the slides are stained and counterstained according to the method of Papanicolaou.

Examination of the esophagus:—The tube is passed to the level of the suspected lesion, which is then lavaged. Abrasive instruments are not needed.

Cytologic examination of the esophagus is indicated in all cases of suspected malignancy. It is contraindicated in the presence of active bleeding.

Examination of the stomach:—It is advisable to aspirate the stomach the evening prior to the examination because asymptomatic retention is frequent in gastric ulcers. The technic is identical to that described above, except that while the stomach is being washed the patient is turned around his long axis a full 360 degrees so that the entire circumference is brought into contact with the solution.

Cytologic examination of the stomach is indicated in gastric ulcer, pernicious anemia and suspected malignancies. It is a valuable aid in the differentiation between malignancies and hypertrophic gastritis. False negative results occur in those cases where a carcinomatous ulceration is covered by an adherent membrane and in those lesions which are completely intramural. The procedure is contraindicated in the presence of very active bleeding.

The following case history shows the value of cytologic examination. A 42-year old white man was first seen in the Outpatient Department because of malaise and a 15-pound loss of weight during the preceding 3 months. On physical examination the entire upper third of the abdomen was found to be tender. X-ray examination of the stomach was not conclusive, while the gastro-

scopic examination indicated either a giant tumor forming gastritis or a polypoid neoplasm. Gastric cytologic examination on three different occasions showed malignant cells. A subtotal gastrectomy was performed. A lesion about 6 by 5 cm. in diameter was found on the greater curvature, which consisted of giant hypertrophic rugae lying over a carcinomatous ulcer like the palm of a hand and completely obscuring the ulcer from view. No obvious nodes were found at the time of operation. Microscopic examination confirmed the diagnosis of carcinoma, but no evidence of nodal metastases was found in the specimen.

Examination of the duodenum:—The preparation for duodenal drainage is the same as that for other upper gastrointestinal procedures, except that we have replaced the end of the tube with a magnetic steel tip which can be pulled into position under the influence of a magnet held on the outside of the body. Our experience has been that we have shortened the time necessary to place the tube with this technic. In some cases the tube could not be positioned without the use of this magnet.

Results of cytological examination of the duodenum have not been as accurate as those of the esophagus or stomach. Since greater accuracy is obtained before any obstruction is present, early cytologic examination of nonicteric patients, as has been emphasized by Lemon[9] and Rubin and his associates[14], is desirable.

The indications for duodenal cytological examination are: 1. suspected malignancy, 2. cases in which there is undiagnosed epigastric distress, even when the x-ray examination is negative, and 3. obstructive jaundice. The procedure is contraindicated in massive gastrointestinal hemorrhage and acute cholecystitis.

Examination of the colon and rectum:—Cytologic examination is unnecessary in lesions accessible to sigmoidoscopic biopsy, with the exception of diffuse papilloma where total surface suction may reveal malignant cells not included in a random biopsy. With the aid of an externally placed magnet, a magnetic-tipped enema tube can reach the transverse and ascending colon.

The indications are as follows: Study of colonic cells is useful in differentiating benign from malignant polyps. It may help to differentiate diverticulitis from carcinoma. This procedure is also indicated in cases with persistent occult blood in the feces in which all other studies have been negative.

The contraindications are acute inflammatory processes and perforation of the colon.

Summary and Conclusions

1. In addition to the routine history, physical and diagnostic roentgen examinations, the gastroenterologist has at his disposal a variety of unique special diagnostic procedures.

2. The safety and simplicity of the Eder-Hufford "flexi-rigid" esophagoscope is stressed.

3. Gastroscopy and gastroscopic biopsy are valuable in select cases.

4. Duodenal drainage is facilitated by using a magnetically positioned tube.

5. The importance of proctosigmoidoscopy, gastric analysis and tests for occult blood in the feces is indicated.

6. The Einhorn string test may localize an obscure bleeding area in the upper gastrointestinal tract.

7. Gastrointestinal cytologic examination is becoming increasingly important as an acceptable gastroenterological diagnostic procedure.

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PRESENT STATUS OF PORTAL DECOMPRESSION FOR PORTAL HYPERTENSION*

CHARLES G. CHILD, III, M.D.

Boston, Mass.

In 1877 Eck proved that in the dog the entire portal blood flow could be diverted into this animal's vena cava by means of an end-to-side portacaval shunt. In his original article, Eck suggested that such a venous fistula as this might be useful in man for the relief of abdominal ascites. Early in this century a few courageous surgeons followed Eck's unique suggestion. Because these early efforts were based upon the misconception that abdominal ascites arose from congestion in the splanchnic venous bed and because surgical mortality proved prohibitively high, success in the early application of the Eck fistula to man was meagre indeed. In 1945, however, A. O. Whipple revived serious interest in portal decompression by reorienting its objective, namely toward preventing hemorrhage from esophageal varices arising secondary to portal hypertension. Esophagogastric varices, McIndoe, McMichael, Whipple and Rousselot contended, developed in response to either an intrahepatic or extrahepatic obstruction to portal blood flow. If the portal hypertension which was produced under either of these circumstances could be effectively reduced to normal, Whipple believed that the devastating hemorrhages which are often a feature of patients with cirrhosis or portal thrombosis could be controlled. Whipple originally described re-introduction of portacaval shunts in man as a "bold attempt to deal with the problem of portal hypertension in its life-threatening forms." Ten years have now elapsed since surgeons in this country and abroad began to follow Dr. Whipple's suggestion. Today a reasonable experience with portal decompression is available for study. It seems appropriate, therefore, to attempt to evaluate the present status of this relatively new approach to the relief of massive hemorrhage from esophagogastric varices.

The accomplishments of portal decompression lend themselves particularly well to consideration under two headings: the immediate and the delayed. The immediate objective of the operation, of course, is to lower abnormally high levels of portal pressure and thereby to prevent variceal hemorrhage. From a review not only of my own data (Fig. 1), but that of others as well, there can be little doubt but that a satisfactory shunt, either portacaval or splenorenal, effectively reduces high portal pressures to normal or near normal levels. At least, portal pressure is reduced to levels at which variceal hemorrhage is rarely,

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From the Department of Surgery of Tufts University School of Medicine and from the First (Tufts) Surgical Service, Boston City Hospital.

if ever, encountered. Furthermore, additional evidence is available indicating that once portal pressure has been reduced it remains at the immediate post-shunt level or falls even further by three to four months after operation. Varices subside (Fig. 2) and enlarged spleens shrink appreciably in size. In addition, such hypersplenism as may have been associated with pre-existing splenomegaly usually disappears. But of even greater importance than either of these immediate hemodynamic manifestations of portal decompression is the fact that further variceal hemorrhage is prevented provided the shunt remains open. In my own series of some 60 patients, none have bled after portal decompression (Fig. 3). This dramatic response to operation mirrors the even larger experience of others.

An immediate effect of portal decompression which cannot, of course, be disregarded is its associated surgical mortality. In this respect, patients with

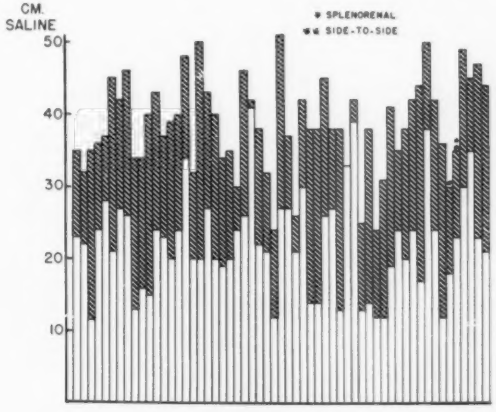

Fig. 1—In this chart pre- and postshunt pressures have been displayed as vertical bar graphs. It is evident that portal pressure falls significantly after opening the shunt. In 56 patients the average fall was equivalent to 20 cm. of saline.

portal hypertension and bleeding esophageal varices may be divided into two groups, those whose obstruction to portal flow is due to extrahepatic thrombosis, and those whose obstruction resides within the liver. In the former group, postoperative mortality has been low—perhaps less than 3-5 per cent, while in the latter it has varied from 10-30 per cent and higher. In my own experience surgical mortality has been 14 per cent for patients whose portal hypertension has been due to one form of cirrhosis or another. The reason for the low mortality in patients with extrahepatic portal block resides, of course, in the fact that they are predominantly young individuals whose hepatic function is good. The higher mortality in patients with cirrhosis is due to the compromised liver function which most of these patients manifest when they become candidates for portal decompression. The variation in reported mortality depends

primarily upon the degree of selectivity exercised. If only those patients with variceal hemorrhage are accepted for operation who have never been jaundiced, who have never been in hepatic coma, who have never had ascites, whose cirrhosis is postnecrotic rather than alcoholic-nutritional, and who maintain a serum albumen level of at least 3.0 gm. per 100 ml., surgical mortality will be low, possibly less than 10 per cent. As soon, however, as one or more manifestations of hepatic decompensation are present, mortality rises appreciably and if caution in selection is not exercised this may prove prohibitive.

Entirely satisfactory solutions to two major problems in the management of the patient with cirrhosis who bleeds have not been found: First, how to

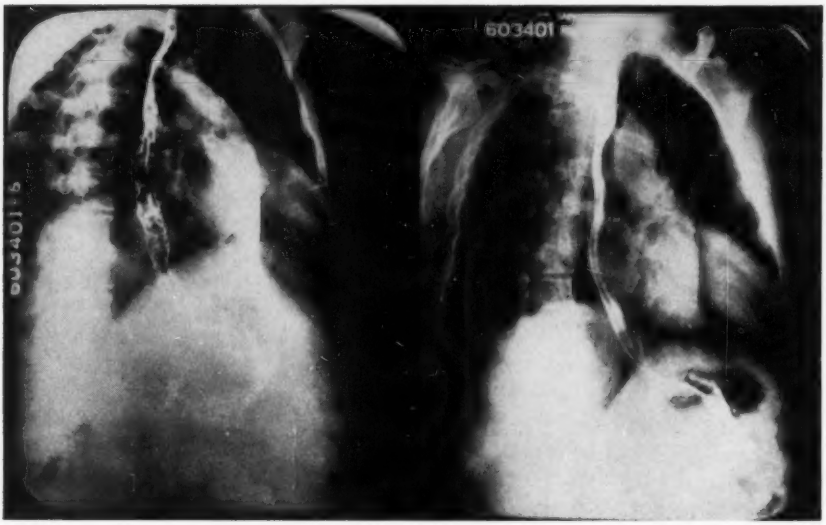

Fig. 2—Reproduction of esophagograms obtained preoperatively and postoperatively in a patient with massive hematemesis from extensive esophageal varices. The roentgenographic return of the esophagus to normal is apparent.

control the acute hemorrhagic episode which is such a major threat to life in these patients; second, how to reduce the surgical mortality to a point where this is not considered a serious deterrent to portal decompression. As far as the immediate control of massive hemorrhage is concerned, pneumatic tamponade has proved life-saving under some circumstances, and has failed in others. When tamponade fails after a reasonable trial, emergent transthoracic ligation of the varices has been disappointing. It is my opinion that a much more productive form of surgical endeavor may be found in promptly subjecting patients in reasonable hepatic reserve to emergency portal decompression (Table I). I do not believe heroic surgical measures are applicable to patients whose

esophagogastric hemorrhages appear in a setting of terminal cirrhosis. With regard to improving surgical mortality, one recent development appears to offer promise, namely that of performing portal decompression under hypothermia. Although experience is small to date, it appears not unlikely that lowering body temperature to 26°-28°C. during operation may reduce the currently high surgical mortality rate encountered amongst admittedly poor risk patients. The significant reduction in the quantity of anesthetic drugs required under hypothermia, as well as a hypothetical decrease in hepatic metabolic demands, may provide just that additional protection which the patient with advanced cirrhosis requires to permit him to undergo portal decompression successfully.

In turning now to the effect of portal decompression upon the long-term survival of patients with portal hypertension and variceal hemorrhage, problems in evaluation are encountered, the solutions to which are not at all clear at this

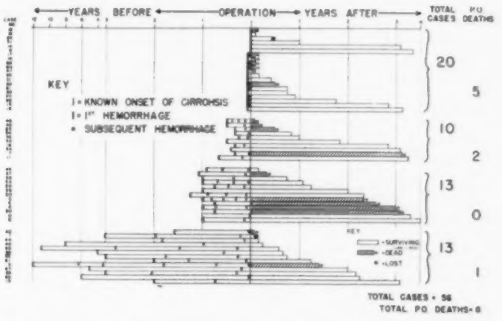

Fig. 3—This figure summarizes the preoperative and postoperative data on 56 patients with cirrhosis subjected to an end-to-side portacaval shunt.

time. Patients whose hemorrhage is secondary to portal thrombosis have a normal life expectancy provided they are protected from the hazards of repeated hemorrhage. These individuals tolerate operation well and do not bleed again provided their shunts remain open. It is unfortunate, however, that in a relatively high percentage of these individuals their shunts close and they bleed again. The reason for this failure is not at all clear, but probably rests with the fact that the splenic vein is less satisfactory for shunting purposes than is the portal. It is also possible that the same factors accounting for the original thrombosis are still effective and predispose this variety of shunt to closure. Nevertheless, the effects of portal decompression on survival in this group of patients has been excellent. Because these individuals are excellent surgical risks a second and even third attempt at decompression is often justified. When all such efforts have failed, esophagogastric resection may be undertaken to prevent further hemorrhage.

In considering the effect of portal decompression upon the survival of patients with cirrhosis who have bled, many complexities make their appearance. For instance, prolonged survival in this group of patients is compromised by the nature of their primary disease. Portal decompression, therefore, at best can only be regarded as a palliative operation. To determine the accomplishments of this operation requires, of course, that some standard be available against which to measure its success or failure. Unfortunately such is not available; at least I do not know of a statistically significant series of patients with cirrhosis who have bled, who have manifested good hepatic reserve and who have refused or who have been denied operation. Nor has the effect of prolonged dietotherapy and cessation of alcohol upon variceal hemorrhage been satisfactorily

TABLE I

EMERGENT END-TO-SIDE PORTACAVAL SHUNT CIRRHOSIS OF LIVER*

Case #	Mos. Surv. to Death	Mos. Surviving	S. Alb. gm./100 ml.	S. Bilir. mg./100 ml.	Ascites
A.—Survived more than one month					
5	17	–	4.0	2.3	+
7	39	–	4.1	6.0	0
25	6	–	3.5	2.7	+
31	–	12	3.6	3.7	+
35	–	9	4.8	8.8	0
B.—Survived less than one month (post op. death)					
26	–	–	2.4	13.5	0
36	–	–	2.6	5.5	+
48	–	–	4.3	32.1	+

*In this table are outlined 8 patients with cirrhosis subjected to emergent portal decompression.

determined. Here and there a few reports can be found indicating that such general hygienic measures as these have been successful in preventing death from further hemorrhage. Evidence in this regard is, however, as yet inconclusive. In brief then it has not been determined whether or not the risk of operation exceeds that of the risk from further hemorrhage. Until this information becomes available there seems little likelihood of determining precisely what the accomplishments of portal decompression in cirrhosis have been.

With so many unknown factors, what logical approach to portal decompression can be taken today? It is my own opinion that, until more information upon the effectiveness of dietotherapy becomes available, patients with cirrhosis who have bled and who are in a reasonable state of hepatic reserve should continue to be accepted for portal decompression. To be defeatistic about the

operation at this point would, I believe, deprive a number of individuals of an opportunity to live useful lives unharassed by the ever present threat of hemorrhage. At the same time, subjecting patients to portal decompression whose hemorrhage is a manifestation of terminal cirrhosis would be unwise indeed. At the present time more detailed follow-up studies are urgently needed, not only upon those who are operated upon, but upon those who for one reason or another are not operated upon. That portal decompression protects from hemorrhage is evident; that the surgical mortality is appreciable is also apparent. Further study is necessary before any final conclusions can be reached as to the usefulness of portacaval shunts in patients with cirrhosis.

Discussion

Question:—I should like to ask a question. Dr. Child, you made a remark that there is a difference between alcoholic and posthepatitic cirrhosis. Do you mind discussing that?

Dr. Child:—At the present time it would be improper for me to give you anything more than a clinical impression in this regard. In an experience with over 100 patients with portal hypertension secondary to cirrhosis, I am convinced that the alcoholic who is still ingesting large amounts of alcohol and whose hemorrhage appears in this setting does not do as well as the patient whose cirrhosis follows hepatitis or other hepatotoxin. Not only does the patient with postnecrotic cirrhosis handle his hemorrhage better, but he also tolerates operation much better.

I am sure that what I am trying to say is this: Given two patients, one a chronic alcoholic and the other an individual who does not drink but whose cirrhosis has followed hepatitis, I will subject the latter to portal decompression with much greater enthusiasm than the former. In addition to his sick liver, the chronic alcoholic is a socio-psychiatric problem as well, who, even though his hemorrhage is controlled by a portacaval shunt, goes on to succumb to his primary disease, his cirrhosis. At the present time my group is trying to document this clinical impression more scientifically but as yet we have been unsuccessful in deriving anything more than that.

DIVERTICULOSIS OF THE GALLBLADDER

D. P. HALL, M.D., F.A.C.S., F.A.C.G.

Louisville, Ky.

Diverticula of the gallbladder are infrequent, although a large single diverticulum has often been found at operation. It is significant that until recently diverticulosis of the gallbladder was not often diagnosed upon roentgenologic examination. Baumgartner[1] in a review of pathologic lesions found in 4,575 gallbladders did not report the finding of diverticula.

There has been much interest in the pathogenesis of gallbladder diverticula especially their interrelation to many diseases of the gallbladder. Rokitansky[2] described outpouchings of the gallbladder mucosa and observed they often contained stones completely separated from the lumen of the gallbladder. Aschoff[3] propounded that diverticula were a causative factor in the pathogenesis of cholecystitis and cholelithiasis but unfortunately he confused diverticula with Luschkas ducts with which the latter conditions are often associated. Aschoff thought that stasis and increased intracystic pressure within a pathologic gallbladder resulted in an increase in the size of the crypts until they were pushed through the muscular coat and became false diverticula, which over a period of time became the habitat of stones.

Halpert[4] supported the idea of Aschoff relative to diverticula being more common in cholecystic disease. He was careful to distinguish between diverticula and Luschkas ducts, the latter he described as aberrant bile ducts which were not related to diverticula.

The observations of many surgeons and radiologists tend to demonstrate that neurogenic disturbances may cause a spasm of the sphincter of Oddi and at the same time initiate strong contractions of the gallbladder wall capable of producing diverticula. In this symptom-complex, biliary colic is an outstanding feature and may occur without infection in the gallbladder wall. When irregular contractions are noted during cholecystography, they may be presumptive evidence of dyskinesia.

It would seem that any abnormality in the biliary ducts or gallbladder itself which exerts increased intracystic pressure might be one of the factors in the pathogenesis of diverticula. One cannot discount the possibility that long standing mild chronic cholecystic disease may be an additional cause for their formation, as a result of obstruction and increased pressure in the gallbladder. MacCarty[5] observed diverticula in 25 gallbladders examined at the Mayo Clinic in a series of 29,701 which were removed surgically between 1893

From the Department of Surgery, University of Louisville School of Medicine and the Kentucky Baptist Hospital, Louisville, Ky.

and 1937. It was his conclusion that diverticula in the gallbladder might be formed in the same manner attributed to diverticula of the stomach, small intestine, colon and appendix.

Glücker[6] remarks that it is somewhat striking that until 1948 no roentgenologic report on diverticulosis appeared, but four cases were recognized by cholecystography in one year in countries separated by long distances. He believes that the roentgen picture is characteristic and the diagnosis can be made in most cases if carefully studied. He is of the opinion that there are certain required conditions for the demonstration of diverticula during cholecystography namely good contrast filling of the gallbladder, a sufficient number of diverticula with wide necks allowing for the easy entry of contrast medium.

Akerlund[7], from his cholecystographic study of the layer formation and sedimentation formation of the gallbladder, has approached the idea that the origin of aseptic cholesterol stones might be ascribed to the crystallization of cholesterol from concentrated residual bile, which has been sedimented in the gallbladder and that diverticula may offer a favorable condition for the retention of such bile and a resultant formation of stones. Gross[8] has stated that a diverticulum may be found anywhere along the free surface of the gallbladder from the fundus to the neck. In the ten cases studied by him the diverticula varied from ½ to 1½ inches in diameter. I am sure that this is probably correct for a single diverticulum but where one has diverticulosis the free surface of the gallbladder may be the seat of diverticula as well as the liver portion of the gallbladder.

There is not a definite symptom pattern in diverticulosis of the gallbladder except by association with cholecystitis or cholelithiasis. One might compare diverticulosis of the gallbladder in the nonproduction of symptoms with benign tumors of the gallbladder which remain symptomless unless complete obliteration of the cholecystic cavity should occur.

Case Report

Mrs. H. O., aged 37 years, was admitted to the Kentucky Baptist Hospital on March 27, 1955, complaining of frequent, intermittent, pain in the epigastrium, of three years' duration not associated with meals. Two months prior to her admission the upper abdominal pain became more severe but at times was relieved by vomiting, of late the attacks have been accompanied by moderate abdominal distention, some indigestion and constipation. A review of various bodily systems reveal no symptoms which might be considered important. She had a panhysterectomy in 1946 from which she made an uneventful recovery, no malignancy was found. A physical examination revealed tenderness in the right upper quadrant of the abdomen but no mass could be palpated. On admission, the temperature was 99, pulse 90, respiration 20 and

blood pressure 118 over 68. The results of urinalysis and blood studies were within normal limits, VDRL negative.

The patient's cholecystogram revealed a fairly good concentration of dye in the gallbladder. There was a waist-like constriction of the proximal third of the body of the gallbladder and considerable irregular opaque materia! in the region of the fundus probably gallbladder mud. The radiographic diagnosis was functioning gallbladder with stones.

At operation on March 29, 1955 chronic cholecystitis with cholelithiasis and diverticulosis of the gallbladder were found (Fig. 1). The gallbladder was

Fig. 1—Diverticulosis of the gallbladder with stones in the diverticula.

adherent to the transverse colon, the wall very much thickened and the fundus felt like a circumscribed tumor. The serosa of the gallbladder was rather pale and numerous blob-like masses presented on its surface. The common bile duct was very thin and the size and color approached an average duct; no stones could be palpated. The color and edges of the liver showed no changes, an exploration of the stomach and duodenum revealed no suspicious lesions.

Cholecystectomy was performed. The postoperative diagnosis was chronic cholecystitis, with cholelithiasis, and diverticulosis of the gallbladder. The

patient made an uneventful recovery and was dismissed from the hospital on April 12, 1955.

Pathologic Examination

Gross Description:—Specimen consists of a gallbladder 10.5 x 4 x 4 cm. The serosa is glistening, edematous and pinkish to slightly greenish gray. The wall is palpably thickened and in the fundus there is a firm, rather rubbery palpable mass. At the ampulla is a small lymph node about 1 cm. in greatest diameter. Extending from the lumen of the ampulla are numerous diverticula up to 5 mm. in diameter, each containing a small black stone. The lumen contains green black bile and multiple irregular black stones. Extending from the lumen in the fundus is an irregular area composed of numerous diverticula varying from 1 to 8 mm. in diameter also containing stones. Grossly, there is no evidence of carcinoma. The mucosa is green and smooth and shows no gross evidence of carcinoma. The wall is edematous, measures up to 1 cm. in thickness.

Microscopic:—Sections of the gallbladder show thickening of the muscular wall, subserosal fibrosis, edema and lymphocytic infiltration and innumerable diverticula extending well through the mucosa into the subserosal area. The diverticula all are lined with perfectly regular columnar epithelium and show no evidence of malignancy. Also sections of the lymph node show chronic inflammatory hyperplasia but no evidence of metastasis.

Diagnosis:—Diverticulosis of gallbladder with chronic cholecystitis and cholelithiasis.

The case here reported supports the view of Aschoff confirming the association of diverticula with cholecystic disease. It may be possible that the contents of these diverticula become a nidus in the formation of gallstones thus supporting the view of Rokitansky.

There is the possibility of cholecystic diverticulosis, because of obstruction and infection, becoming the primary cause in a few suppurative conditions of the gallbladder. An inflammatory process in an acute cholecystitis may completely mask the diverticula.

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THE EFFECTS OF A LOW FAT DIET ON THE INCIDENCE OF GALLBLADDER DISEASE*

LESTER M. MORRISON, M.D., F.A.C.G.

Los Angeles, Calif.

During the course of a 10-year program of metabolic studies in coronary atherosclerosis, the author noted corollary findings of clinical interest in the management of gallbladder disease. This report presented before the Annual Convention of the American College of Gastroenterology is a preliminary one with emphasis on the effects of diet in the treatment of gallbladder disease.

The results of long-time study of the value of a low fat-low cholesterol diet in the treatment of coronary atherosclerosis were first reported in a series of 100 controlled patients by Morrison[1]. It was again reported by Morrison[2] that following 8 years of continued dietetic treatment of coronary atherosclerosis in the controlled series of patients who had survived a coronary thrombosis with myocardial infarction, rate of prolongation of life was increased over 100 per cent in the dietetically treated patients as compared with the control patients who did not adhere to the low fat-low cholesterol diet.

The author noted that no incidence of known gallbladder disease or symptoms developed in any of the dietetically treated patients with coronary disease and healed myocardial infarction, over an 8-year period of time. This was in sharp contradistinction to the customary development of gallbladder disease in patients with coronary disease as noted in current textbooks and clinical experience. As a consequence the author was stimulated to explore further this interesting clinical observation.

In addition to the above series of 100 controlled patients, the author extended these observations to an additional series of 100 patients over a 10-year period of time. These latter cases were not patients with coronary thrombosis and myocardial infarction but were of the general character encountered in the private practice of internal medicine such as cases of obesity, peptic ulcer, colitis, hypertension, psychoneuroses, hypercholesterolemia, etc. The patients were placed on a 25 gm. daily dietetic fat intake, cholesterol intake of 75 mg.; the protein intake ranged from 75 to 125 gm. and the carbohydrate intake from 100 to 200 gm. daily. A supplement was administered daily in the form of a standard multivitamin preparation ensuring adequate Vitamin A intake, as well as other vitamin supplements such as whole wheat germ and

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brewer's yeast as required for optimal nutrition. This diet is representative of the one originally proposed by Morrison[1] in previous publications for the treatment of coronary atherosclerosis[2,3].

A control series of 100 non-dieting patients treated by the author was observed under the same circumstances with the same general character of illness and over the same 10-year period of time.

As shown in Table I, of the 100 patients on the low fat-low cholesterol diet for 10 years, only 1 patient developed gallbladder dyspepsia and distress. This 55-year old man had 4 brothers who died of coronary thrombosis; the patient had hyperlipemia, was resistant to therapy and died following a coronary thrombosis. Autopsy revealed a pathological gallbladder with cholelithiasis. In the 100 patients observed while on their uncontrolled customary American dietary fat intake, 8 patients developed the gallbladder syndrome, 3 requiring cholecystectomy during the 10-year period. Gallbladder symptoms were those

TABLE I

INCIDENCE OF GALLBLADDER SYNDROME IN 200 PATIENTS OBSERVED FOR 10 YEARS

Treatment	Number of Cases	Cases with Gallbladder Attacks or Disease	Verification	Incidence
Dietetically treated Low fat-Low cholesterol diet	100	1	Autopsy	1%
"Controls"—No special diet	100	8	Surgery (3) X-ray (8)	8%

as typically encountered, consisting of epigastric and/or upper right quadrant pain in attacks or with recurrent distress, gasseous eructations, pyrosis, fat or fried food intolerance, flatulence, nausea or vomiting of bile, constipation, etc. All 8 patients in the "control" group had x-ray evidence of pathological findings such as cholelithiasis with or without impaired gallbladder functional power.

The ages for the dietetically treated group ranged from 36 to 75 years and for the "control" group without dietary control from 33 to 74 years. No specific gallbladder medication was used in either group. The distribution of sexes were similar in each group, there having been 38 males and 62 females in the dietetically managed series and 35 males and 65 females in the dietetically managed series in the "control" series without dietary control.

The average weight losses for both sexes in the dietetically treated series were significant and virtually identical with that reported in the comparable

series of coronary thrombosis patients treated by the author[1,2] (male–average weight loss, 21 lbs.; female–average weight loss, 17 lbs.). The falls in total serum cholesterol levels were substantial and practically the same as previously reported (average total blood serum cholesterol fall, 92 mg.). These are the subjects of a report to follow. It is of clinical interest to note in passing that the majority of patients in the dietetically treated group continually remarked on their sense of well-being, increased exercise tolerance and improved capacity for work.

Comment

The near absence or 1 per cent incidence of gallbladder syndrome in 100 patients adhering to a low fat-low cholesterol diet (10 years) as compared to the 8 per cent incidence or eight-fold increase for the 100 patients on an uncontrolled dietary intake draws attention to the question of gallbladder disease etiology in this country and under our current eating and living habits.

Since the vast majority of cases of gallbladder disease are associated with the presence of gallstones to which the clinical disorders are in the main attributable it would be of interest to note the 3 main factors which have been incriminated in gallstone formation. These are: 1. Infection of the bile or gallbladder wall. 2. Changes in the composition of the bile. 3. Bile stasis.

Regarding the first factor of infection, Morrison et al[4-7] investigated this aspect as follows.

Special and separate cultures were made from the different layers of the gallbladder wall, from the cystic gland, and from the gallbladder bile in a series of 20 surgically resected gallbladders. All 20 gallbladders were diagnosed pathologically as "cholecystitis", either "acute" or "chronic". The cultures were sterile in 18 out of 20 cases so studied. Two positive cultures were obtained from patients with empyema of the gallbladder associated with cystic duct obstruction.

Intravenous injections of heavy suspensions of streptococcus and *Escherchia coli* failed to cause cholecystitis in any of a series of rabbits, though the rabbits were injected twice weekly for from 4 to 8 weeks. This result suggests that cholecystitis is not due solely to blood-borne organisms. This evidence indicates that in the majority of cases infection does not play a primary role in producing cholecystitis.

These findings have recently been amply corroborated by numerous investigators[8-10]. The factor of infection should therefore be considered as a secondary one. The factor of bile stasis has been generally conceded to apply mainly to pregnancy cases and is now adjudged to be of secondary importance.

The second etiologic factor stated above, changes in the composition of the bile remains apparently the cardinal one in the etiologic consideration of gallbladder disease and gallstones, as found by various observers[8-10] and by Morrison[4-7] in a series of investigations. It is well known that three main biliary elements enter into gallstone synthesis, viz., 1. cholesterol, 2. bilirubin and 3. calcium. These are formed most often by bile rich in cholesterol and poor in bile salts, diseased gallbladder mucosa and biliary stasis. There result physiochemical changes in the bile leading to the precipitation and crystallization of the above constituents out of the biliary colloidal menstruum. The exact or specific factor or "trigger" mechanism is not yet known, but it is now clear that the primary factors in gallbladder disease and/or gallstone formation are metabolic in origin. All other factors such as inflammation and infection are secondary.

In view of these metabolic considerations the importance of diet in the etiology and management of gallbladder disease and stones is manifest.

TABLE II

BILE COMPOSITION OF GALLBLADDERS AT ABDOMINAL LAPAROTOMY IN DISEASED AND NONDISEASED GALLBLADDERS

State of Gallbladder	Number of Cases	Average Concentration of Bile Salts	Average Concentration of Cholesterol	Ratio of Bile Salt Concentration to Cholesterol	Average Blood Total Cholesterol
Cholecystolithiasis	28	440 mg./100 c.c. bile	42 mg./100 c.c. bile	10	315 mg./100 c.c. blood
Normal*	16	850 mg./100 c.c. bile	18 mg./100 c.c. bile	47	236 mg./100 c.c. blood

*Aspiration from Gallbladder at Laparotomy for Nonbiliary Tract Diseases.

In previous studies, Morrison[5,6] found that a prolonged intake of a high fat diet resulted in an increased concentration of cholesterol in the bile and a diminution of bile salt concentration in the bile (human subjects). This was accompanied by an increase in total blood serum lipids and cholesterol. From the author's studies it was noted that when the bile salt-cholesterol ratio falls below the ratio of 13, precipitation out of cholesterol from the bile occurs and gallstone formation with or without cholecystitis is initiated. In human bile it was found that the normal bile salt-cholesterol ratio was 20 to 50, a figure delicately close to the critical point of cholesterol precipitation and indicative of what sensitive balance the bile constituents are held.

In previous reports[4-7] the author described the bile salt concentration in the bile by stalagmometric means as the most delicate indication of hepatic

cell function. It was then noted that the prolonged high dietary fat intake was more frequently associated with a trend to suppression of bile salt concentration in the bile plus a tendency toward increased bile cholesterol concentration. The fatty acid concentration in the bile also played a significant role in maintaining the normal equilibrium of bile salts and cholesterol. When fatty acids were increased, bile salts were increased and cholesterol was suppressed and prevented from crystallization or precipitation out of the bile (Table II).

Evidence was presented that gallstone formation is associated with suppression of bile salt concentration in the bile in the majority of the gallstone cases studied in this series. It is an exclusive function of the liver to maintain the bile salt concentration in the bile. Hepatic dysfunction causes suppression of the bile salt concentration in the bile. The bile salt concentration in the bile is suppressed by a group of agents, or their combinations.

These agents are: 1. biliary tract infection, 2. biliary tract stasis, 3. diets high in fat content over prolonged time periods, 4. pregnancy, 5. organic liver disease, 6. avitaminosis, 7. hereditary factors, 8. biliary dyskinesia (psychosomatic factors?), 9. infectious diseases such as typhoid fever, 10. repeated recurrence of fevers, 11. chemical agents, as sulfanilamide and 12. metabolic factors.

Summary and Conclusions

One hundred patients were observed over a 10-year period while on a low fat-low cholesterol diet and compared to 100 patients who acted as controls and who were consuming a typical American unrestricted diet. Both series of patients consisted of both sexes with age ranges from 33 to 75 years.

The incidence of gallbladder disease or symptoms was almost nil (1 per cent) in the dietetically treated series of patients and was eight times greater in the unrestricted diet group of control patients.

Studies of bile chemistry revealed that high fat dietary intake was associated with increased cholesterol content of the bile and suppression of bile salts in the bile.

Suppression of the bile salt concentration in the bile causes precipitation of cholesterol and calcium bilirubin pigment with the production of gallstones.

These studies suggest that low fat diets, such as those followed in certain Asiatic countries, are responsible for the absence or low incidence of gallbladder disease in those countries.

These findings also suggest the advisability of low fat dietary intake in patients who have cholelithiasis or who have had surgical procedures for gallstones within the biliary tract.

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SOME PERPLEXITIES IN THE PROBLEM OF JAUNDICE

LOUIS J. VORHAUS, II, M.D.
New York, N. Y.

We can do more to investigate the liver than almost any other organ in the body, and yet find ourselves perplexed with the differential diagnosis of jaundice more often than almost any other of the standard puzzlers in clinical medicine. Nowhere, it has been emphasized, does a careful history prove more rewarding. Nowhere are there as many little telltale physical findings to act as guideposts to the meticulous examiner. Nowhere do we have such a plethora of tests and measurements. No other organ is as readily and frequently subjected to biopsy. And lastly, time is on the doctor's side, for rarely does the situation demand an immediate decision, so, if in doubt, one can always wait and see what happens. Yet day in and day out, the differential diagnosis of the jaundiced patient continues to baffle the intern, professor and practitioner alike. For with all the facilities at our disposal, the solution is still impossible to come by, in about 5 to 10 per cent of jaundiced patients.

By solution, of course, is meant the decision as to whether to treat the patient medically or surgically, for this is the crux of the matter. If, for example, a patient can be diagnosed as having extrahepatic obstruction, that is enough—at operation the cause can be determined and dealt with, for all will agree that extrahepatic obstruction is a surgical problem. On the other hand, we also will all agree that the best treatment for hepatitis is certainly not general anesthesia and laparotomy.

Why is the problem so difficult? Why with all these diagnostic facilities can we not make the diagnosis, particularly when we don't even need to pin-point it? The answer is simply this: Jaundice is seldom a simple matter, caused by a single type of disturbance. Many cases of extrahepatic obstructive jaundice have associated hepatocellular damage either from back pressure or infection particularly if the jaundice lasts for any extended period of time. Many cases of hepatocellular disease are accompanied by obstruction of the finer intrahepatic biliary radicles due to edema and swelling of the liver cells or stasis of bile plugging the canaliculi, or a combination of both, and many are accompanied by an anemia due to increased blood destruction. And finally, many hemolytic anemias may be complicated by factors which cause obstruction or hepatocellular dysfunction.

Pure obstruction, pure liver cell disease or even pure hemolytic anemia are, in fact, much less common than at least some admixture of them. Unfortunately it is those cases which are clearly defined clinically that give unequivocal laboratory tests, while the cases which are more bizarre, atypical and confusing clinically give confused laboratory data. To this must be added that

while we know, by and large from experience, which tests signify increased blood destruction, which signify obstruction and which hepatocellular disease, we really know relatively little about what's going on with them or what they are *really* testing. As a matter of fact, we don't even understand too much about bilirubin metabolism, though a few years back it all seemed quite simple.

We know that bilirubin is a product principally of hemoglobin breakdown. A small amount (probably 10 per cent or so) comes from other sources such as myoglobin, the cytochromes, etc. While it was once thought that the liver manufactured the bilirubin, it is now generally agreed that the reticuloendothelial cells (in spleen, bone marrow, etc.) carry on this function[1,2] by a process of oxidation which can be reproduced *in vitro*[3]. Thus the hemoglobin molecule, containing four heme molecules plus a globin molecule is split, the heme molecule (a protoporphyrin, composed of four pyrrol rings plus iron) is opened, with production of verdohemoglobin. Subsequently the iron is split away and bilirubin released into the circulating blood[4]. What happens subsequently has been a subject of much inconclusive investigation and even more dispute. It has been said that there are few fields in biochemistry where so much work has been done with so little success[5]. It has long been known that bilirubin circulates, is excreted or more correctly actively secreted by the liver[6] and goes with the bile into the gut. Back in 1913 van den Bergh noted that there were differences between bilirubin that had not yet been secreted by the liver and bilirubin that was to be found in bile[7]. The bilirubin in bile (which appears in the urine when its blood level rises), gave color in the diazo reaction, whereas the bilirubin in blood (which does not spill over into the urine) required treatment with ethanol before it would react. The difference, subsequently labelled direct and indirect van den Bergh, was thought to be due to the fact that prehepatic bilirubin was bound to a protein from which it was split on passage through the liver (or with ethanol treatment). In subsequent years the van den Bergh reaction was more accurately modified into prompt-reacting or one minute bilirubin (which corresponds to the direct van den Bergh) and the delayed-reacting or 30-minute bilirubin (corresponding to the indirect van den Bergh)[8]. It was felt that this difference in bilirubin would prove useful in distinguishing different types of jaundice, a feeling, as will be discussed later, that has proved disappointing. The subject, however, has provoked much investigation into the nature of the difference between direct-reacting and delayed reacting bilirubin. It is generally agreed that the bilirubin, released by the reticuloendothelial cells, becomes attached to protein (probably globulin)[9]. What happens at the liver is not so certain. It has been variously claimed that nothing happens (the difference in direct and indirect reacting bilirubin depending on such physical factors as salt concentration, nature of the proteins, pH, etc.)[5-10] that it is split from globulin and converted into a sodium salt (sodium bilirubinate)[11], that it is combined with a metal (attaching to albumin

if it gets back into the bloodstream)[8], that its nature is somehow changed in some manner, as indicated by differences in solubility and in crystalline form[11-14] and that it is transformed into two new and different pigments[2]. Whatever happens in the liver the hepatic cells have to actively work to clear it of blood[6]. The question of whether this is the only method by which the body can clear the bloodstream of bilirubin is intriguing. It has often been observed in cases of proven complete biliary obstruction that the jaundice does not become intense, and occasional instances have been noted where jaundice was completely lacking. In no case does it continue to rise indefinitely though red cell destruction does not cease and urinary loss can never fully account for all the bilirubin that should be derived from normal hemoglobin destruction. This suggests the possibility that, when necessary, the body is capable of breaking down bilirubin through alternate channels (which appears to be the case when ACTH or cortisone administration to jaundiced patients causes a reduction in serum bilirubin)[15-17], or that hemoglobin under such circumstances is converted to something other than bilirubin[18]. The occasional finding of nonpigmental bile (white bile) in the common duct may support this possibility, though it may on the other hand reflect an inability of the liver to secrete bilirubin[19].

Whatever happens to the bilirubin on passage through the liver, it ends up in the bile and, barring obstruction, enters the gut where further reduction takes place under the influence of intestinal bacteria[20]. While the various pathways of bilirubin reduction are not entirely worked out, it appears fairly certain that bilirubin is reduced to either d-urobilinogen or dihydromesobilinogen. Then either of these is converted to mesobilinogen. Further reduction can go to urobilinogen or stercobilinogen and probably other compounds as well. Stercobilinogen can be converted to stercobilin or possibly to urobilinogen[21,22]. The subsequent enterohepatic circulation of urobilinogen is well known—urobilinogen is partly reabsorbed from the gut and reexcreted for the most part by the liver in the bile, a small fraction being excreted through the kidney[23].

Jaundice occurs when, for any reason, bilirubin is not properly cleared from the bloodstream and discolors the skin and sclerae by virtue of its elevated levels in the blood and its penetration into the tissues. The only conditions which may give rise to confusion are carotinemia or after atabrine administration[24]. It may vary from intense to being almost imperceptible, and one may have a mild elevation of serum bilirubin which cannot be detected at all. By and large, while the normal level of serum bilirubin is under 1.0 mg. per cent, jaundice cannot be observed clinically until a level of 1.5 to 2.0 mg. is reached. When jaundice is minimal it may be detected only under daylight and will be missed if looked for under the yellow tint of artificial illumination. Due to the affinity of elastic tissue for bilirubin, it is often detected in the sclerae before the skin becomes noticeably yellow[25].

Many classifications of jaundice have been proposed, but generally the most useful is to think in terms of prehepatic, hepatic, and posthepatic. In prehepatic there is either an excessive destruction of hemoglobin (hemolytic anemias) or an elevation in threshold of bilirubin clearance by the liver (physiologic hyperbilirubinemia or familial nonhemolytic icterus). In both of these conditions, all of the bilirubin elevation is of the indirect or delayed reacting type, and therefore there is no bile in the urine. Neither should present diagnostic difficulties if borne in mind. Hemolytic anemias present fairly classical hematologic findings, including increased urinary and fecal urobilinogen output, increased reticulocytes in the peripheral blood, and a hyperactive marrow. On liver biopsy, increased amounts of iron are generally noted in Kupffer cells. It is important to remember, however, that a relatively low grade hemolytic process may be going on with little or no anemia. The bone marrow is able to respond with an increase in blood cell production. While normally the marrow turns out about 0.09 gm. of hemoglobin per kilogram per day, it may increase the output to 0.6 gm. per kilogram per day (or up to 45 gm. a day). Thus, an anemia will appear only if destruction exceeds this augmented output[26]. The picture in the prehepatic jaundice of hemolytic anemia may be complicated by other factors which can lead to confusion in diagnosis. Many patients suffering with a chronic hemolytic anemia are subject to development of biliary pigment calculi due to the high concentrations of bilirubin in their bile[23], and if one lodges in the common duct it may cause obstructive (posthepatic) jaundice. Furthermore the patient with chronic hemolytic anemia may require frequent, multiple transfusions and ultimately develop transfusional hemosiderosis, which may add the factor of hepatic jaundice to the prehepatic type[29,30]. Finally, in the face of a severe anemia, the associated anoxemia may affect the hepatic cells so as to impair their function[23].

Physiologic hyperbilirubinemia, another form of prehepatic jaundice, is a somewhat rare condition encountered in apparently healthy people. It seems to be familial and is usually first noted in childhood. Serum bilirubin rarely exceeds 3 mg. per cent, and all studies of liver, spleen, bone marrow and blood are normal. Probably due to a functional impairment of hepatic bilirubin clearance, it tends to clear with advancing years[27,28].

In hepatic jaundice, the disease is obviously within the liver, due to liver cell damage, whether of infectious, toxic, nutritional, or metabolic origin. Posthepatic (or obstructive) jaundice implies a block beyond the liver cell. It was once thought that hepatic and posthepatic jaundice were terms synonymous with medical and surgical jaundice. The sorry fact is that this is not the case. Obstruction may occur anywhere from the most minute bile canaliculi to the ampulla of Vater, and may therefore be within the liver, as part of a hepatitis or cholestasis, as well as outside, from a gallstone or a carcinoma of the head of the pancreas. As already suggested, prolonged obstruction invariably causes liver damage from back pressure and/or ascending infection. It is, therefore,

the problems involved in delineating the obstructive from the hepatocellular and differentiating the surgical from the medical jaundice that may confound even the wisest and most experienced clinician.

In the process of working up a case of jaundice, the importance of a careful and thoughtful history and physical examination has been stressed frequently, for if all the available clues are detected and all the signposts followed, a correct diagnosis should be reached in 70 to 80 per cent of cases[31,32]. So far as the general points in the history go, age is helpful in that obstruction from stone or neoplasm is uncommon under the age of 40 while hepatitis is usually seen in younger individuals. Sex is of less importance, though certain of the diseases causing jaundice have a definite sex incidence (as gallstones are more common in females while cirrhosis and carcinoma of the pancreas are seen more often in men). More important are the details regarding the patient's background, occupation, etc. Thus the cleaner may be exposed to carbon-tetrachlorides which may cause liver damage while the plumber or sewer worker may come in contact with rats carrying Weil's disease. History of medications may be revealing, as a variety of drugs may cause hepatitis with cholestasis (as arsenic, sulfonamides, methyltestosterone or thorazine), while parenteral administration of blood or blood products may be followed by serum hepatitis. A history of alcoholism coupled with nutritional inadequacy suggests the possibility of cirrhosis, while a patient who has long suffered with flatulence, fatty food intolerance, or chronic indigestion may have a common duct stone. Previous surgery for cancer may point to hepatic metastases, while a history of exploration in the region of the common duct points to the possibility of a postoperative stricture. The details of the present illness also are of utmost importance. The nature of onset (sudden or gradual, painless or painful, presence of systemic or gastrointestinal symptoms such as malaise, low grade fever, anorexia, nausea or vomiting, or the absence of such associated symptoms) often leads to correct diagnosis[33]. If pain is present, it is important to determine its characteristics—vague discomfort in the right upper quadrant aggravated by jarring suggests hepatitis, severe colicky pain points to gallstones, while deep midepigastric pain radiating to the back raises the question of pancreatic pathology. Severe itching is much more frequently encountered in obstruction than hepatocellular disease. Other things, such as the color of stool and urine, presence of hematemesis or melena, and recent changes in weight (either increase or decrease) may give further useful clues[34].

On physical examination there is further information to be gleaned[35]. Stigmata of cirrhosis (as soft skin, loss of chest, axillary and pubic hair, venous telangectasia, spider angiomata, gynecomastica, testicular atrophy) are generally apparent. Adenopathy may suggest neoplasm. Ascites, splenomegaly, varices, and increased abdominal collateral circulation are not commonly seen in obstructive jaundice (except occasionally with widespread metastatic malignancy

where the diagnosis is obvious)[36]. Liver size is not too helpful as there may be considerable hepatomegaly with prolonged obstruction. A large liver early in the course of jaundice, however, certainly favors hepatic disease. A palpable gallbladder, on the other hand, generally signifies obstruction[37].

The laboratory work-up should only be undertaken after the history and physical examination have been thoroughly completed. Of the 20 to 30 per cent of cases not already diagnosed, about half of them will be clarified by the laboratory. A huge number of liver function tests have been proposed as useful guides in differential diagnosis[6]. Flocculation tests (as the cephalin flocculation, thymol turbidity, thymol flocculation, zinc sulfate turbidity, Takata-Ara, and so forth) indicate the presence of abnormal globulins due to mesenchymal activity, and suggest hepatocellular disease. Serum albumin levels and serum cholinesterase activity provide guides to total functioning liver mass. Alkaline phosphatase excreted by the liver, is helpful in that levels over 15 Bodansky units indicate obstruction. A rise in total cholesterol suggests the same thing, while a drop in cholesterol, particularly in the esterified fraction usually accompanies liver cell damage[38]. Levels of bilirubin are not helpful in differential diagnosis, and, while in hemolytic processes, there is a definite rise in the indirect delayed-acting fraction, partition is of no value in distinguishing hepatocellular from obstructive jaundice[39,40].

X-rays may be useful. Scout film of the abdomen may show gallstones. Barium swallow may reveal esophageal varices, displacement of the stomach from retrogastric nodes, or distortion of the duodenal sweep from pancreatic neoplasm. And while the oral technics of gallbladder visualization are of no value in the jaundiced patient, the more recent intravenous methods may be helpful when the jaundice is of low grade intensity[41].

Lastly liver biopsy may give a diagnosis when all other methods fail, in about 5 per cent of jaundiced cases[42].

When no diagnosis can be reached by all methods available, the physician is justified in closely watching for a while to see what will happen. Often in a matter of a few weeks the question will be resolved by the patient's course. If, however, confusion still exists after four to six weeks, the patient is entitled to exploration for at this stage more harm can come from neglecting a patient with extrahepatic obstruction than exploring one suffering with hepatocellular damage[27].

In the long run it is wise clinical judgment, combined with careful study that will produce the best batting average in the jaundice problem. The search for newer and better liver function tests will doubtless continue, and with each passing year more will be added to the battery already in use which may help the clinician a little more. But, as long as multiple factors are at work to produce jaundice, liver function tests will never provide a substitute for thoughtful

clinical appraisal, based on detailed history, thorough physical examination, and judicious use of laboratory aids combined with an understanding of the underlying mechanisms at work.

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THE ASSOCIATION OF LIVER DISEASE WITH ULCERATIVE COLITIS

HARRY J. KANIN, M.D.
JACK J. LEVIN, M.D., F.A.C.G.
Wood, Wisc.
and
M. C. F. LINDERT, M.D.
Milwaukee, Wisc.

Introduction

The incidence of liver disease in patients with ulcerative colitis has been pointed out in recent medical literature. The purpose of this paper is to report findings of a study of 29 cases of ulcerative colitis to determine the incidence of hepatic involvement, and the histologic pathology in the livers of six cases of ulcerative colitis which came to autopsy.

TABLE I

	No. Cases Tested	No. Cases Abnormal	% Abnormal
Bromsulfalein	11	9	82
Zinc sulfate	6	4	66
Alkaline phosphatase	6	3	50
Thymol turbidity	11	3	27
Total serum cholesterol	7	3	43

Review of the Literature

There is a lack of valid statistics as to the true incidence of liver disease in ulcerative colitis. Jones et al[2], found abnormal bromsulfalein retention in 50 per cent of 24 cases of ulcerative colitis. After performing liver biopsies on six patients without clinical evidence of liver disease, Bargen[1] found abnormalities in four. Hoffbauer, et al[3], reviewing 287 autopsies of ulcerative colitis found 12 cases of cirrhosis of the liver. They considered this an unusually high incidence.

Fatty infiltration is the most frequently reported liver alteration. Other types of liver pathology which have been found in cases of ulcerative colitis are post-

From the Medical Service, Veterans Administration Hospital, Wood, Wisc., and Department of Medicine, Marquette University School of Medicine, Milwaukee, Wisc.

necrotic cirrhosis, Laennec's cirrhosis, pericholangitis, necrosis, interlobular hepatitis, multiple bile casts, and focal areas of inflammation[4].

Most authors to date believe nutritional deficiency to be the primary etiological factor of liver disease in ulcerative colitis[4]. Specifically, hypoproteinemia has been found to be associated with fatty infiltration of the liver[2]. Dyson[5] believes that deficiency of methionine and cystine leads to fatty infiltration, which progresses to cirrhosis. Kimmelstiel, et al[6], classified the hepatic lesions found in these cases into two types, degenerative and inflammatory. They concluded that the degenerative lesions (fatty infiltration, cirrhosis, etc.) were

TABLE II

Ulcerative Colitis
With Abnormal Liver Function Tests

	Age of Patient	Duration of Symptoms in Months	Severity of Symptoms	Extent of Colon Involvement by X-ray or Proctoscopy
1.	38	84	Mild	Rectum Only
2.	29	72	Moderate	Distal ½ of Colon
3.	40	144	Severe	Entire Colon
4.	31	12	Moderate	Examination Unsatisfactory
5.	25	6	Severe	Entire Colon
6.	35	36	Severe	Entire Colon
7.	56	252	Moderate	Distal ½ of Colon
8.	35	60	Moderate	Rectum and Sigmoid
9.	31	24	Mild	Entire Colon
10.	37	120	Mild	Distal ½ of Colon
11.	32	4	Mild	Distal ½ of Colon

caused by nutritional deficiency, and that the inflammatory types of lesions (i.e, hepatitis, periportal foci of inflammation) were due to toxins carried from the bowel to the liver through the portal system.

Presentation of Data

The records of 63 unselected cases of ulcerative colitis, who had been hospitalized at the Veterans Administration Hospital, Wood Wisc., were reviewed. Liver function tests were performed on 29 of these cases. Eighteen of the 29 showed normal liver function; 11 of the 29 manifested laboratory evidence of

liver disease—an incidence of 38 per cent. One case had clinical evidence of liver disease manifested by jaundice and a palpable liver.

In the 11 cases showing abnormal liver function tests, the bromsulfalein was found to be most frequently altered. Results of this and other tests are recorded in Table I.

TABLE III

ULCERATIVE COLITIS
WITH NORMAL LIVER FUNCTION TESTS

	Age of Patient	Duration of Symptoms in Months	Severity of Symptoms	Extent of Colon Involvement by X-ray or Proctoscopy
1.	27	84	Moderate	Entire Colon
2.	37	120	Moderate	Entire Colon
3.	41	72	Moderate	Distal ½ of Colon
4.	28	36	Moderate	Distal ½ of Colon
5.	63	36	Severe	Rectum and Sigmoid
6.	28	7	Mild	Rectum and Sigmoid
7.	30	60	Severe	Entire Colon
8.	59	120	Severe	Distal ½ of Colon
9.	22	42	Moderate	Entire Colon
10.	26	48	Moderate	Entire Colon
11.	31	1½	Moderate	Entire Colon
12.	26	24	Moderate	Entire Colon
13.	52	15	Mild	Distal ½ of Colon
14.	31	96	Severe	Entire Colon
15.	33	84	Severe	Entire Colon
16.	22	36	Severe	Entire Colon
17.	31	36	Moderate	Entire Colon
18.	35	72	Moderate	Distal ½ of Colon

A liver biopsy was done on the case presenting jaundice, an enlarged liver, and a bromsulfalein retention of 17 per cent. Laennec's cirrhosis was found.

Microscopic examination of the liver was also done in 6 cases of ulcerative colitis which came to autopsy. The reports are as follows: Fatty degeneration in 2;

fatty infiltration and chronic passive congestion in 1; parenchymatous degeneration and chronic passive congestion in 1; biliary stasis in 1; and normal liver in 1.

Two of the autopsied cases had had liver function tests during their hospitalization. One case showing fatty infiltration had a bromsulfalein of 11 per cent, total serum cholesterol of 92, and serum albumin of 2.54. The case showing a normal liver had had a bromsulfalein retention of 13 per cent.

The average duration of ulcerative colitis in the 11 cases showing abnormal liver function tests was 51 months. The average duration of disease in the 18 cases showing normal liver function was 54 months. In both groups, the extent of involvement of the colon varied from localized to generalized, and the activity of the disease varied from mild to severe. Our observations agreed with the finding of Kleckner[7], that the duration, activity, or extent of involvement of the colon with ulcerative colitis could not be correlated with the incidence, type, or severity of associated liver disease (Tables II and III).

Summary

A study was made to determine incidence of liver disease in patients with ulcerative colitis. Thirty-eight per cent of all 29 cases reviewed showed abnormal liver function tests. Only 1 of the 29 cases manifested clinical evidence of liver disease. Of 6 autopsied cases reviewed, microscopic examinations revealed pathologic livers in 5.

No correlation was found between the incidence of liver disease and the duration or extent of the ulcerative colitis.

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EDITORIALS

"Irritable Colon"—A Bad Term

In the present day of advance in the etiology and manifestation of diseases and disorders, it is well to discard useless terms and make the effort to describe organ disturbance as accurately as possible. The days of blanket terms or presenting symptoms of disorders under entity terms has long since passed, and while such may be satisfactory to some, they lack in elucidation to others and are especially restrictive to the advance of a good or scientific medicine.

A term that never should have been coined and should be discarded is "irritable colon" or "unstable colon" which occurs so often throughout medical literature and medical reports. It was born not many years ago as a "baggage" term to include a lot of common disorders of the colon. Not much interest in the different types of colon disorders was present at the time so an all-inclusive term was devised and since has spread about in general usage and no attention was paid to the fact that it not only means nothing, covers a good deal of ignorance, but is a confusing nuisance in addition.

One hundred reports in which one of these terms occurred were studied as to what was the most feasible diagnosis. A little more than half of these occurred in reports from hospitals usually from the X-ray Department. While a roentgenologist is not expected to be a diagnostician of accurate differentiation of functional colon disorders, it must be kept in mind that the functions of the colon are easily upset and that disturbance situated in any part of the body could disturb colon function. Identification of the colon state in cause and effect is not always possible, but in such an instance it would be logical to consider the colon state as resulting from the organic disease, rather than consider it an entity of its own. This brings forward the importance of careful examination in all instances of colon disorder.

In the breakdown of these 100 cases in which the term "irritable colon" was used, organic disease in various parts of the body was met with. Of these there were 41. One may argue here that an organic disease and functional colon disorder could occur together, one being in no way connected with the other. While such may be possible, the tendency was to make no connection between the two. There is no excuse here for reporting "irritable colon" any more than reporting an organic lesion of the colon as constipation or chronic diarrhea. It would be far better to report the change in function or anatomy and leave the clinician to interpret it in clinical ways.

The nonhospital reports came from men who were engaged in the practice of medicine, some even from gastroenterologists who should be more accurate. At times the terms were used without an x-ray examination. Of these 59 cases no corporeal disease could be discerned and the cases were judged as more

particularly of colon origin. Even here, however, emotional neurologic, bad routine, biotoxic intestinal states, ptosis, nutritional disturbances, etc., were present in all but 9 cases.

One may now ask the question, "Is it not far better, more scientific and truer to clinical fact not to use the terms "irritable" or "unstable" colon and to use the broader diagnosis, even if some of the older terms like atonic, spastic neurosis, are used instead?"

ANTHONY BASSLER, M.D., F.A.C.G.

IMPROVED ANESTHESIA FOR GASTROSCOPY

Gastroscopic examinations are at times incomplete or unsatisfactory because of the inherent discomfort to the patient. Most gastroscopists employ some type of preliminary sedation followed by a varied list of anesthetic agents. Topical applications of pontocaine, gargling with pontocaine or cocaine solutions are supplementary procedures in common usage. More recently intravenous demoral has been employed by some gastroscopists. General anesthesia with pentothal has been used on very infrequent occasions. In our experience these methods of inducing anesthesia have not been uniformly satisfactory for gastroscopic examinations.

In an attempt to reduce the patient's discomfort by more effective anesthesia during gastroscopy, we have employed inhalational analgesia by mask with trichlorethylene*. The degree of relaxation and decrease in the patient's discomfort has been so marked in most instances, that we feel that this should result in wider use of this valuable diagnostic procedure in indicated cases. These observations will be reported in more detail in a subsequent publication.

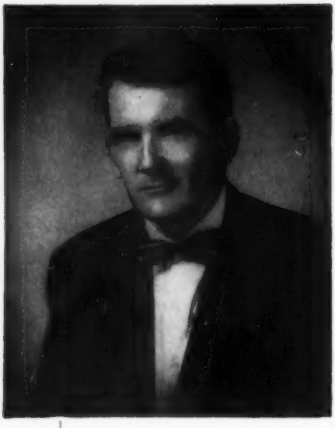
MILTON J. MATZNER, M.D. F.A.C.G.

*"Trilene"—Ayerst Laboratories.

In Memoriam

We record with profound sorrow the passing of Dr. Roy Upham of New York, N. Y., Fellow and esteemed Secretary-General of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved family.

Tributes to the late Dr. Upham will be published in an early issue of THE AMERICAN JOURNAL OF GASTROENTEROLOGY.



President's Message

Your Board of Trustees has selected New Orleans, Louisiana, as the site of the next regional meeting of the American College of Gastroenterology. Dr. Louis Ochs, Jr., chairman of the local program committee, has enlisted the assistance of our men in the southern states in planning an exceptional program for 8 April 1956.

Included in this program are papers on aberrant pancreatic tumor, ulcerative colitis as seen in the southern states, pathogenesis and management of hepatic coma, and massive gastrointestinal bleeding. Guest speakers include: Dr. I. W. Kaplan, Dr. C. A. Jones, Dr. J. R. Snavely, Dr. C. J. Miangolarra and Dr. Alton Oschner.

This year the Louisiana group has decided to inaugurate the Abraham L. Levin Memorial Lectureship in conjunction with the regional meeting. This lectureship is in memory of our late, renowned confrère, Dr. Abraham L. Levin who, in 1921, developed the stomach tube that now bears his name. Dr. Levin was head of the gastroenterological section at the Louisiana State University School of Medicine and was the founder of the Louisiana Chapter of the National Gastroenterological Association. The initial paper of this lectureship is to be "Advances in Ulcerative Diseases of the Gastrointestinal Tract" by Dr. Asher Winkelstein.

Hope to see you in New Orleans in April.

I. T. Nix

NEWS NOTES

Books For Foreign Library

We are in receipt of an urgent plea from Dr. T. K. Thomas, Medical Superintendent, St. George's Hospital Library, Punalur, P. O., Travancore, S. India, for books on gastrointestinal diseases for use in the library. Dr. Thomas writes that 75 per cent of the patients coming to the mission hospital are suffering from some type of gastrointestinal disease, and literature on the subject is desperately needed.

Copies of The American Journal of Gastroenterology have been sent gratis to Dr. Thomas for the past year, and if any readers can forward books or enter subscriptions to other journals for the library, it will be greatly appreciated.

Eighth Annual Convention—International Academy of Proctology

The 8th Annual Teaching Seminar of the International Academy of Proctology will be held at The Drake, Chicago, Ill., April 23 to 26, 1956. The International, National, and Local Program Committees are planning an unusual seminar on anorectal and colon surgery. There will be special emphasis on anorectal presentations, and on panel discussions, as requested by those who attended the New York meeting in 1955.

Eminent speakers from all parts of this country and abroad will present interesting papers and motion picture demonstrations of their personal technics. Mexico is expected to be very well represented at this meeting.

The Women's Auxiliary has planned a very unusual program for the wives of the members and their guests.

All physicians and their wives are cordially invited to attend the Annual Teaching Seminars of the International Academy of Proctology, whether or not they are affiliated with the Academy. There is no fee for attendance at these teaching sessions of the Academy.

International Society of Geographic Pathology

The 6th Congress of the International Society of Geographic Pathology will be held in Paris, in July or September of 1957.

The subject for the conference will be "The Geographic Pathology of Peptic Ulcer". Plans call for a world wide study of peptic ulcer and the international committee in charge of arrangements would welcome participation by as many investigators from America as possible. Further information and questionnaire forms for the national study may be obtained from William B. Wartman, Secretary American Section, International Society for Geographic Pathology, Northwestern University Medical School, 303 E. Chicago Avenue, Chicago 11, Illinois.

REGIONAL ACTIVITIES

PROGRAM

SOUTHERN REGIONAL MEETING
AMERICAN COLLEGE OF GASTROENTEROLOGY
Sunday, 8 April 1956

BUSINESS SESSION

JUNG HOTEL

New Orleans, La.

9:00 A.M. Meeting of the Board of Trustees of the American College of Gastroenterology

12:30 P.M. Board of Trustees Luncheon.

SCIENTIFIC SESSIONS

Auditorium

LOUISIANA STATE UNIVERSITY SCHOOL OF MEDICINE

New Orleans, La.

FIRST SESSION

DR. JAMES T. NIX, President, American College of Gastroenterology, presiding.

2:00 P.M.

1. "Massive Gastrointestinal Hemorrhage."

Speaker

DR. CHARLES J. MIANGOLARRA, Clinical Professor of Surgery, Louisiana State University, School of Medicine, New Orleans, La.

Discussion opened by:

DR. MURREL H. KAPLAN, Senior in Department of Gastroenterology, Touro Infirmary, New Orleans, La.

2:30 P.M.

2. "Problems and Management of Ulcerative Colitis as Seen in New Orleans."

Speaker

DR. CHARLES A. JONES, Chief of Medicine, Veterans Administration Hospital, New Orleans, La.; Associate Professor of Clinical Medicine, Tulane University School of Medicine, New Orleans, La.

Discussion opened by:

DR. DONOVAN C. BROWNE, Associate Professor of Clinical Medicine, Tulane University, New Orleans, La.

3:00 P.M.

3. "Aberrant Ectopic Tissue in Stomach."

Speaker

DR. I. W. KAPLAN, Clinical Professor of Surgery, Louisiana State University, School of Medicine, New Orleans, La.

Discussion opened by:

DR. MEYER D. TEITELBAUM, Clinical Associate Professor of Radiology,

Louisiana State University, School of Medicine, New Orleans, La.

3:30 P.M. Intermission

SECOND SESSION

DR. LOUIS OCHS, JR., Chairman, Board of Governors, American College of Gastroenterology, presiding.

3:50 P.M.

4. "Value of Proctoscopy as a Part of Routine Physical Examination."

Speaker

DR. ALTON OCHSNER, Director of Surgery Division, Ochsner Clinic, New Orleans, La.; the William Henderson Professor of Surgery and Chairman, Department of Surgery, Tulane University, New Orleans, La.

Discussion opened by:

DR. SAMUEL KARLIN, Clinical Assistant Professor of Surgery, Louisiana State University, School of Medicine, New Orleans, La.

4:20 P.M.

5. "Etiology and Therapy in Hepatic Coma."

Speaker

DR. ROBERT SNAVELY, Professor of Medicine, University of Mississippi Medical School, Jackson, Miss.

Discussion opened by:

DR. E. L. POSEY, JR., Posey-Stephenson Clinic, Jackson, Miss.; Consultant in Gastroenterology, Veterans Administration Hospital, Jackson, Miss.

4:50 P.M.

6. "Operative Cholangiography."

Speaker

DR. PAUL D. ABRAMSON, Chief of Surgery and Breast Service, Tumor Clinic, Confederate Memorial Hospital, Shreveport, La.

Discussion opened by:

DR. HERMAN RABIN, Department of Surgery, Touro Infirmary, New Orleans, La.

EVENING SESSION

8:00 P.M.

FIRST ABRAHAM L. LEVIN MEMORIAL LECTURE

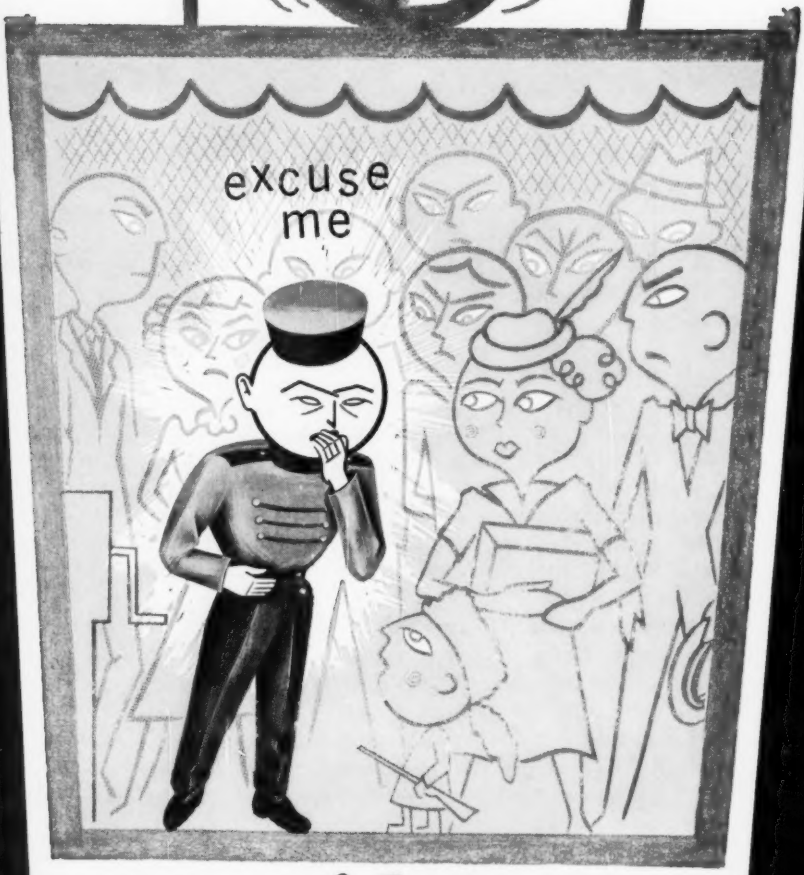
Introductory remarks by:

DR. ISIDORE COHN, SR., Clinical Professor Emeritus of Surgery, Louisiana State University, School of Medicine, New Orleans, La.

"Recent Advances in Ulcerative Diseases of the Gastrointestinal Tract."

Speaker

DR. ASHER WINKELSTEIN, Assistant Clinical Professor of Medicine, Columbia University, College of Physicians and Surgeons; Consulting Gastroenterologist, The Mount Sinai Hospital, New York, N. Y.



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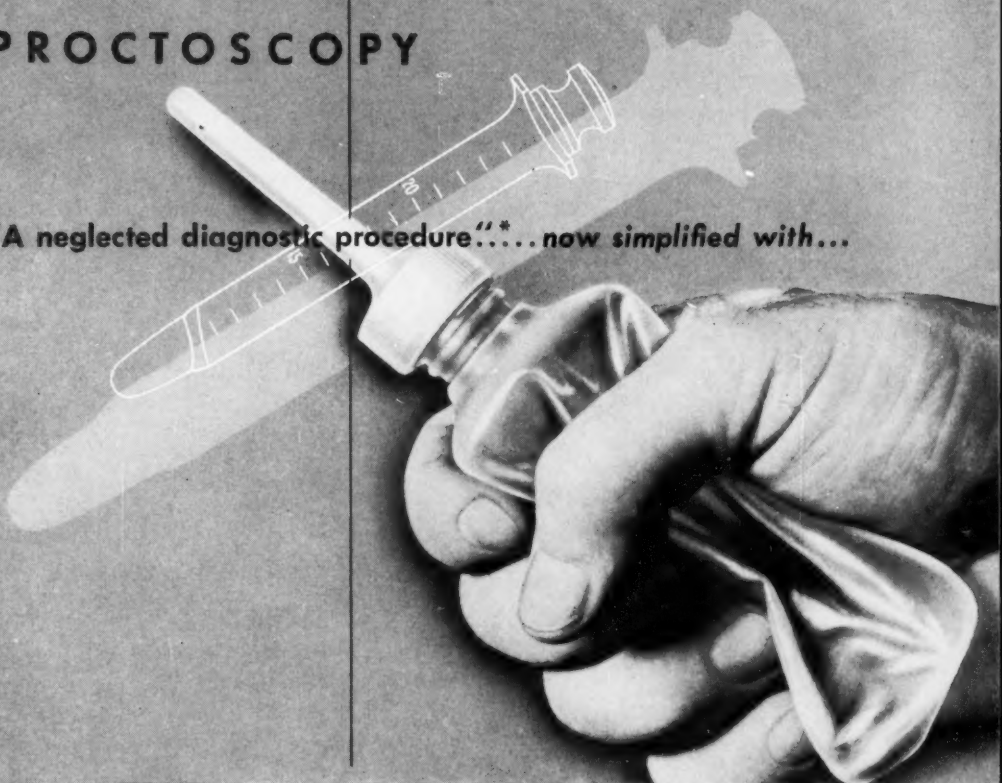

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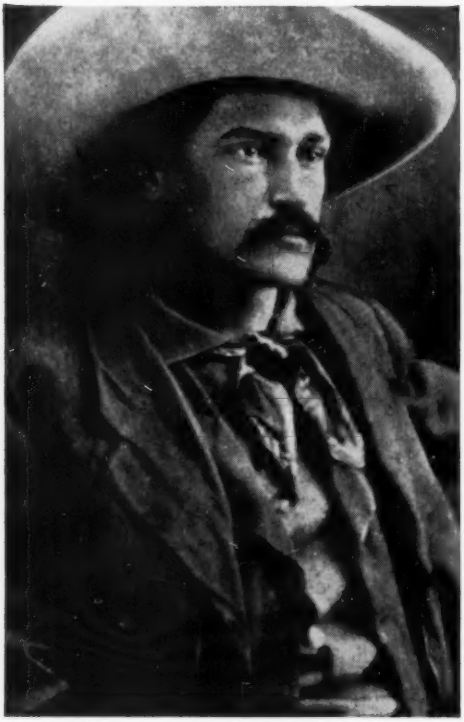
- Xylocaine Viscous has proved valuable in the "dumping" syndrome, hiccup, pyloric spasm caused by peptic ulcer, stomatitis, pharyngitis, esophagitis, acute cardiospasm, pylorospasm in infants, severe vomiting of pregnancy, esophagoscopy, gastroscopy, gastric intubation and gastric lavage.
- Contains 2% Xylocaine Hydrochloride in an aqueous solution adjusted to a suitable consistency with carboxymethylcellulose. Cherry flavored for palatability.

Supplied: In bottles of 100 and 450 cc.
Average Dosage: One tablespoonful, administered orally.
Additional information available upon request

ASTRA

Astra Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.

*U.S. Patent No. 2,441,498



His calling card had claws on it

LUTHER KELLY lied about his age and got into the army at 15. They sent him West in 1865, and he stayed.

He liked the wilderness. Game abounded. In Trappers' Lake, "trout were so thick they obscured the bottom."

Hostile Indians were also pretty thick. But when two tried ambushing him, he killed both with his Henry .44.

He learned Sioux and sign language, read Shakespeare and Scott.

One day, he visited General Miles, sending a huge fierce-clawed bear's paw to Miles' tent as his calling card. Miles made him chief army scout against the Sioux.

But by 1885, the country was taming down, and Yellowstone Kelly left it.

Two decades later, Teddy Roosevelt praised the heroic treasurer of Surigao in the Philippines who saved the town from outlaws. Name: Luther S. Kelly.

Yellowstone Kelly's body now rests at Kelly Mountain in Montana. But his restless, pioneering spirit lives on in today's America. For it is the trail-blazing courage of 165 million people that makes America great, and that provides the real strength behind one of the world's finest investments: our country's Savings Bonds.

Why not guard your security with this strength? Invest in U. S. Series E Savings Bonds. And hold on to them!

It's actually easy to save money—when you buy Series E Savings Bonds through the automatic Payroll Savings Plan where you work! You just sign an application at your pay office; after that your saving is done *for* you. The Bonds you receive will pay you interest at the rate of 3% per year, compounded semiannually, when held to maturity. And *after* maturity they go on earning 10 years *more*. Join the Plan today. Or invest in U.S. Savings Bonds regularly where you bank.

Safe as America—
U.S. Savings Bonds

Cremomycin.

SULFASUXIDINE® – NEOMYCIN SUSPENSION WITH PECTIN AND KAOLIN

new – for prompt diarrhea control, quick return to work

MAJOR ADVANTAGES: Combines 'Sulfasuxidine' with neomycin for broader antibacterial action. Pectin and kaolin have soothing, detoxifying properties. Fruit flavor tastes good.

In diarrhea–whether specific or nonspecific–prompt relief is assured with CREMOMYCIN. 'Sulfasuxidine' and neomycin have a wide range of effectiveness–their combined action is complete and prompt, and they are virtually nontoxic.

In addition to the antibacterial components, kaolin and pectin in CREMOMYCIN provide adsorbent and detoxicant action, soothe inflamed intestinal mucosa. The fine subdivision of all ingredients in CREMOMYCIN increases its efficacy.

Each fl. oz. (30 cc.) of CREMOMYCIN contains 3.0 *Gm.* 'Sulfasuxidine,' 300 *mg.* neomycin sulfate, 0.3 *Gm.* pectin and 3.0 *Gm.* kaolin. Supplied in 8 oz. bottles.

SHARP & DOHME

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DIVISION OF MERCK & CO., INC.

new... paired piperidol action
for functional gastrointestinal complaints

rapid
visceral eutonic, Dactil*

prolonged
cholinolytic, Piptal†

relief throughout the G. I. tract

Tridal

TRIDAL permits more comprehensive control of gastrointestinal complaints by providing the combined benefits of two piperidols. The local action of Dactil* works immediately to give **rapid** relief of gastrointestinal pain and spasm; the potent cholinolytic Piptal† reinforces relief and provides **prolonged** normalization of secretion and motility.

TRIDAL is singularly free from urinary retention, constipation, dry mouth, blurred vision.

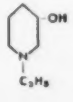
dosage: One TRIDAL Tablet two or three times a day and at bedtime. Unless rapidly swallowed with water, TRIDAL will produce some lingual anesthesia.

Each TRIDAL Tablet contains 50 mg. of Dactil and 5 mg. of Piptal. Bottles of 50 compressed, uncoated tablets.

*Dactil (the *only* brand of N-ethyl-3-piperidyl diphenylacetate hydrochloride): the piperidol to prescribe alone when no interference with digestive secretion is desired.

†Piptal (the *only* brand of N-ethyl-3-piperidyl-benzilate methobromide): the piperidol to prescribe alone when peptic ulcer is known to be present and normalization of secretion as well as motility is desired.

Lakeside Laboratories, Inc. PIONEERS IN PIPERIDOLS MILWAUKEE 1, WISCONSIN



93196

New . . . fastest

tastiest . . .

broad-spectrum

TETRABON*

BRAND OF TETRACYCLINE

and broad-spectrum, vitamin-fortified

TETRABON SF†

BRAND OF TETRACYCLINE HYDROCHLORIDE WITH VITAMINS

homogenized mixtures

ready to use . . .
readily accepted . . .
rapidly absorbed . . .
(therapeutic blood levels
within one hour) . . .
rapidly effective . . .

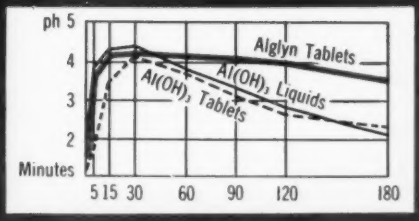
Delicious, unusual blends specially homogenized to provide therapeutic blood levels within one hour. 125 mg. tetracycline per 5 cc. teaspoonful. Tetrabon SF provides, in addition, the vitamins of the B complex, C and K recommended for nutritional support in the stress of infection.

Bottles of 2 fl. oz., packaged ready to use.

*Trademark
†Trademark for Pfizer-originated, vitamin-fortified antibiotics

Pfizer PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N.Y.

Announcing Revision of N.N.R. Monograph for



2

ALGLYN®

dihydroxy aluminum aminoacetate

On the basis of considerable *in vitro* evidence accumulated over a period of seven years, the Council on Pharmacy and Chemistry has revised the original ALGLYN monograph acknowledging that this most recent form of aluminum antacid therapy is as active—IN TABLET FORM—as the various aluminum hydroxide preparations are in LIQUID form:

> "Dihydroxy aluminum aminoacetate . . . shares the properties of the aluminum hydroxide gel preparations. *In vitro* studies indicate that the buffering action of dihydroxy aluminum aminoacetate in tablet form is comparable to that of the liquid preparations of aluminum hydroxide gel when compared on the basis of equivalent aluminum content."

Alglyn Tablets, 0.5 Gm. dihydroxy aluminum aminoacetate, are supplied in bottles of 100 (white). Your patients will welcome the change from liquid antacid preparations to easy-to-take convenient, lightly-flavored Alglyn Tablets.[1]

Also supplied in combination with spasmolytic and sedative therapy as **Malglyn Compound,** each tablet contains dihydroxy aluminum aminoacetate, 0.5 Gm., belladonna alkaloids, 0.162 mg., phenobarbital, 16.2 mg., per tablet, bottles of 100 (pink); and as **Belglyn,** dihydroxy aluminum aminoacetate, 0.5 Gm., belladonna alkaloids, 0.162 mg., per tablet, bottles of 100 (yellow).

Reprint of recent *in vivo* studies available on request

1. Rossett, N.E. and Rice, M.L. Jr.: Gastroenterology, **26**:490, 1954.
2. Hammarlund, E.R. and Rising, L.W.: J. Am. Pharm. Assoc., Scientific Edition, **38**:586, 1949.

Brayton **PHARMACEUTICAL COMPANY**

CHATTANOOGA 9, TENNESSEE

sugar and spice and . . . gastric hyperacidity

Nice to taste . . . difficult to digest . . . the result, more often than not, will be gastric hyperacidity. Bad experiences and good intentions notwithstanding, this particular chain of misfortune is likely to recur. With Gelusil, however, excessive gastric acidity – whether acute or chronic – can be quickly and pleasantly relieved.

Sustained antacid action: The sustained action of magnesium trisilicate and specially prepared aluminum hydroxide gel restores and maintains a mildly acid gastric pH, without over-neutralizing or alkalizing. Gelusil thus avoids the twin dangers of acid rebound and systemic alkalosis.

Non-constipating: Gelusil's aluminum hydroxide component assures a low aluminum ion concentration; hence the formation of astringent – and constipating – aluminum chloride is minimal.

Dosage: 2 tablets or 2 teaspoonfuls two hours after eating or when symptoms are pronounced. Each tablet or teaspoonful provides: 7½ gr. magnesium trisilicate and 4 gr. aluminum hydroxide gel.

Gelusil®

ANTACID • ADSORBENT

WARNER-CHILCOTT